Body, Mind, and Sugar

Body Mind and Sugar

E. M. Abrahamson, M.D.
and A. W. Pezet

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To

Doctor Seale Harris

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Body, Mind, and Sugar

Introduction

MEDICAL SCIENCE has made great progress in the twentieth century Despite its advances, however, the mysteries still outnumber the certitudes The number of medical papers that begin, "We do not know what," "We do not know why," and "We do not know how," is still formidable Medical men do not like to admit this to laymen They have invented words and phrases—neurosis, neurasthenia, and psychoneurosis with depression—to hide their ignorance from the layman and from themselves

Are the hundreds of thousands, perhaps millions, of people thus labeled suffering from mental or from physical disease? The vast majority of them wander from general practitioner to specialist to psychiatrist without ever finding a cure for the ailments that make their lives a misery to themselves and an irritation to those close to them

Almost daily one reads of a hitherto considered sane person who has run amuck and killed someone Even more common are reports of persons who have committed suicide for no reason other than "depression" There are approximately eight thousand murders and twice that number of suicides in the United States every year Not all of the murders are gang murders, premeditated killings, or accidents Recently, for example, it was pointed out that of a hundred indicted

murderers defended by Judge Samuel Liebowitz in his days as a defense attorney not one had a criminal record They were people who had killed 'in a moment of insanity" And the list of persons who have recently killed themselves while suffering from a psychoneurosis with depression' reads like a page torn from *Who's Who*

Since physicians are required to report only communicable diseases, statistics on those suffering from such afflictions as hay fever, asthma, rheumatic fever, and peptic ulcer are not available. The number suffering from the various allergies grouped under hay fever must be enormous It is large enough for a daily pollen count to be taken throughout North America during the hav fever season and for newspapers to publish the results Everyone knows that hay fever and asthma are in some way related, that hay fever sufferers often become asthmatics as they grow older, and that asthmatics get worse and die In the normal sense, however, asthma is not a fatal disease, but rather one that lingers until death/For rheumatic fever the direct death rate is low, 0 8 per 100,000 for the year 1946 (the latest for which complete statistics are available), but the rate from heart ailments that result from chronic rheumatic fever is twenty times higher Stomach ulcers, as they are popularly called cause as many deaths a year as murder Cancer of the digestive organs is one of the half dozen greatest causes of death, the number of malignant tumors located in the insulin secreting islets of the pancreas is only a small fraction of this total.

In the United States there are approximately four million men and women who could be classed as alcoholics They cannot drink as normal people do Their drinking is compulsive In advanced cases, once they start drinking they cannot stop until the alcohol supply is expended or until they finally pass out What is it that sets these persons apart from their normal fellows?

Doctors and employers alike are becoming aware of the

increasingly large number of people who suffer from chronic fatigue These people are too tired or too apathetic to do their work, whether occupational or household duties, with satisfactory efficiency

Pick up a newspaper and you will read of the brilliant pitcher who had a near no-hitter going until the seventh or eighth inning and then "blew up" You will read also of the railroad engineer with the impeccable record of many years who drove past the red signal and wrecked his train

Why are the greatest number of industrial accidents bunched between mid and late afternoon?

Is there any mental or physical basis for the moral breakdown that underlies all delinquency and crime?

Now these diseases and conditions and happenings and questions appear utterly unrelated It is the purpose of this book to show you their very close relationship indeed, the result of recent discoveries of their common conditioning

These discoveries have been made in the laboratory and by means of the scientific method They have been verified by other workers and recognized in at least one instance by honoring the discoverer with one of the highest awards in the medical field But the almost obvious implications of these discoveries are still a matter of controversy and not as yet accepted by the medical profession as a whole, largely because most doctors have not as yet had time to read the literature

Indeed, not all of those whose brilliant thinking and patient labors have contributed to these determinations are aware of the work of others in the same field In several cases it was the lay member of this collaboration who revealed the existence of parallel work to isolated researchers

This is not surprising Scientists often attack similar research projects from vastly different directions Their work frequently is published in journals devoted to a different speciality And today the literature in any scientific field is so

vast that no man busy working in it, especially the physician with his private and clinical practice, can possibly assimilate it all

It is also a normal part of what sociologists call "the cultural lag" that new knowledge is slow to influence the behavior of even the minority who can "think" Today, however, we are living at a rate of change so rapid that our very survival may depend upon the speed with which we are able to take ad vantage of new knowledge No apology is needed, then, for a book that attempts to disseminate such knowledge

The subject matter of this book should be the personal concern of more than ten million people at the very least It is quite possible that their number may be as great as thirty million, one fifth of our population We have no idea how *many persons may be affected in other countries*

Moreover, the factor that brings all these remote and unlikely things together in one category of conditioning, if not of causation, may be the golden key that will in time unlock the closed doors of many other mysteries

A few years ago Behaviorism was the fashion Man was an animal and nothing more His mental processes were but functions of a brain conditioned by external physical stimuli Now the pendulum has swung to the opposite extreme Physicians write articles with such titles as Your Mind Can Control Your Body" The word *psychosomatic*, in which the psychic *is* placed before the physical only for reasons of euphony, is misinterpreted to give the psychic precedence over the physical

When doctors and laymen have fully digested the dis coveries of the last quarter century to which we call attention in this book, we believe they will agree that all arguments about which is cause and which effect—the body or the mind —are as groundless as the age old problem of the chicken or the egg Body and mind are inseparably interrelated The

mechanism of their relationship is to be found in the nervous system and the ductless glands

This book is about the extraordinary part that blood sugar plays in the mechanism that keeps body and mind in healthy balance

About ourselves the medical half of our collaboration E M Abrahamson received his doctorate in chemistry in 1922 and in medicine in 1926 Author of *Office Clinical Chemistry* (Oxford University Press 1945) he has contributed more than a score of papers to medical and chemical journals He also is the designer of several pieces of laboratory apparatus now used in the fields of clinical medicine and chemistry A specialist in diabetes for many years he has devoted much of his efforts toward clinical research and treatment in hyperinsulinism

The lay member of our collaboration A W Pezet was trained at the Massachusetts Institute of Technology and at Harvard University and is a professional writer of both fiction and nonfiction In the latter field he has specialized in writing on medical and other scientific subjects for the layman

This book was conceived through a doctor patient relationship—Abrahamson having diagnosed Pezet and his wife as being victims of hyperinsulinism The lay member of our collaboration experienced more than clinical interest in this diagnosis and in the ensuing treatment Why had he wandered through countless consultations and diagnoses and treatments for more than a decade without relief from his curious symptoms? Why was so little known about a disease condition which affected millions? Why had so little information reached the practicing physician? Why?

The "why s" went unanswered this was not the first time that the field of medicine had procrastinated in making use of its own knowledge

The lay member was determined that a knowledge of hyperinsulinism and its ramifications should be made available to the many who were suffering as he and his wife had suffered The medical member had already written some half dozen scientific monographs on the subject, published in various medical journals, he had long wanted to present the facts to the layman and to the physician unreached by the technical treatises '

The result this book It has been written in language understandable to the layman It is hoped, however, that those physicians who may read this will be impelled to consult our sources and to investigate further the theses which we present

E M A
A W P

New York City
July 18, 1951

1

"... But I Cannot Name the Disease"

There is a sickness
Which puts some of us in distemper but
I cannot name the disease

—THE WINTER'S TALE Act I Scene 2
Camillo

AT ABOUT two o'clock one cold February morning in 1935 I (Dr Abrahamson) was called to a patient who was undergoing an attack of paroxysmal tachycardia—a sudden disturbance of the heart causing it to beat at an extremely rapid rate

When I arrived the young man was gasping for breath and his chest vibrated with the rapid movements of his heart His pulse was so fast that I was unable to count it A quick examination failed to disclose any anatomical trouble I tried the usual procedures that are supposed to halt such attacks—pressing the eyeballs pinching the back of the neck and applying pressure over the carotid arteries in the neck—but the seizure continued I finally had to administer morphine

Within a few minutes the heart resumed its regular rate and the young man was quite comfortable I then thoroughly examined his heart and finding nothing wrong with it told him that the attack was not serious Since there was no organic

defect in his heart he would recover completely without any permanent ill effects I assured him that he would probably never have another attack

A few nights later he had another attack Again morphine was required to stop it Again examination revealed nothing and again I assured him that he would no longer be bothered According to what I had studied I explained many persons experience one or two such attacks and then are permanently free of them

But my patient s heart had not read the medical books and the poor fellow continued to suffer attacks several times a week Why he remained under my care is beyond me for I was certainly a prophet without honor After a few weeks I suggested that he consult a heart specialist There was a serious risk of addiction from the repeated injections of morphine

In those days almost any doctor who owned a cardiograph was considered a heart specialist But I sent my patient to a cardiologist of unquestioned eminence He examined my patient physically and with the electrocardiograph He wrote me a letter confirming my diagnosis of "cardiac neurosis I was greatly pleased that this outstanding specialist had reached the same conclusion as I Now that I have matured in medicine however I have come to realize that I had merely covered my ignorance with a glib phrase Cardiac neurosis means a nervous condition which manifests itself by affecting the heart But what exactly is a nervous condition? My patient was a neurotic (a diagnosis sometimes made by doctors who do not know what is wrong with their patients)

The thing to do then was to send my patient to a psychiatrist He would find out what made my patient nervous" and would remove the hidden cause The neurosis" would disappear and *with it the palpitation It all sounded fine* My patient went to a psychiatrist

At that time I was interested in diabetes and was associated

with two large diabetes clinics, one of which I headed. Diabetics are treated with injections of insulin to keep the blood sugar level reasonably close to the normal, the dosage is controlled by determining the sugar content of the blood at fairly frequent intervals. I was setting up the apparatus in my laboratory one afternoon when my patient called me. He was suffering a frightful attack and had to leave his office. He was coming to see me and he would remain until I discovered what was wrong with him, once and for all. It was to be my last chance.

When he arrived, I frankly did not know where to begin. He was panting and I could see the rapid pulsations of the blood vessels in his neck. He was furious, and I had to do something to pacify him, if nothing else. I took him into the laboratory and drew a sample of blood, which I analyzed for sugar. The analysis would take about half an hour—enough time, I hoped, to think of *something!*

The normal fasting blood sugar (that is, in the morning before breakfast) lies between 60 and 120 milligrams of sugar per 100 cubic centimeters of blood. During the day, while food is consumed, it rises to about 140 mg. per 100 cc. When I finished the analysis, I was shocked to find that his blood sugar level was only 52 mg. per 100 cc.! I repeated the determination. It checked.

Now at last I knew why he had these attacks. A similar symptom occasionally occurred in my diabetics when their blood sugar levels fell too much as the result of an overdose of insulin. The condition was called insulin shock. Whenever a diabetic suffered such an attack we administered sugar. Hurriedly I mixed some glucose with water and lemon juice and gave it to my patient to drink. His palpitation stopped within five minutes.

My patient told me how well he now felt. He also related his experiences with the psychiatrist. This was the per[iod] when unbridled Freudianism was in its heyday. It [w]

fashionable to have a complex or two The libido, which was discussed only in whispers and only in the inner sanctum of the psychiatrist (the term is now freely used even on the radio), was at the bottom of all our troubles The patient's subconscious *was explored and his libido exhumed The* young man was gravely informed that he had a complex—his subconscious had produced these attacks so that he would have an excuse to avoid his wife My felonious diagnosis—cardiac neurosis—which had been attested to by the cardiologist was now compounded by the psychiatrist

Now I knew all the answers My patient had a deficiency in blood sugar Logically there was but one thing to do feed him sugar It had stopped the seizure right before my eyes And usually his attacks occurred in the small hours of the night long after his last meal when his sugar reserves were depleted *So I prescribed disks of dextrose Ordinary* hard candy disks are made from cane sugar which must be converted into dextrose (another name for glucose) and levulose *by the digestive apparatus before it can be absorbed by the* blood By using dextrose one step would be eliminated

My patient bought a box of these tablets and went home He telephoned me from time to time that he still had attacks quite frequently but that they yielded promptly to the tablets Soon, however he reported that the attacks were occurring more frequently Now he bought the dextrose disks by the case He had to take them several times an hour He was unable to sleep through the night Soon he placed a dish of the tablets on his night table before retiring During the night he would reach over and take one almost without waking He *was eating so much dextrose that he was becoming positively* obese

I could not understand why he was unable to rid himself *of the attacks After all, I was following sound physiological* reasoning His blood sugar dropped he had an attack He took some glucose, his blood sugar rose The attack stopped But

that was not the end of the chain. The attacks persisted in repeating themselves.

One day, however, I came across an article by Dr. Seale Harris, professor of medicine at the University of Alabama. I wrote to Dr. Harris telling him of my patient and asking for help in treating him. Dr. Harris kindly sent me some reprints of his work. It was then that I realized how I had mistreated my patient, and that unwittingly I was responsible for his failure to get well.

Sugar taken into the stomach raises the blood sugar. By using glucose (dextrose) the rise in blood sugar is even more rapid because the glucose does not require digestion. It is absorbed through the walls of the stomach directly into the blood stream. The sudden rise in blood sugar stimulates the production of insulin. My patient had *hyperinsulinism*. His insulin tissue was too sensitive and was overgenerous. Instead of making only the amount of insulin needed to handle the amount of sugar just taken into the blood, an excess of insulin was produced, causing another drop in his blood sugar. His symptoms returned and with them a demand for more glucose. The vicious circle! I treated my patient according to Dr. Harris' directives and he soon completely recovered.

[illegible]

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It was through this long suffering patient that I met *hyperinsulinism*, the opposite of *hypoinsulinism*, which is another name for diabetes, the disease I had specialized in for so many years. The golden key had been placed in my hands but I was still far from fully understanding its use. It is necessary to go back in medical history if Dr. Harris' concept and its implications are to be appreciated.

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2

The Old: Diabetes—

ARETAEUS AND "THE LADDER"—THE ISLANDS OF LANGERHANS—INEVITABLE DEATH—BODY AND SUGAR—INSULIN—DIABETIC *COMA—THE GLUCOSE TOLERANCE* TEST

MAN'S KNOWLEDGE of the diseases that afflict him has grown slowly and most unevenly At first a person just "got sick" as wild animals do He either recovered or died The first doctors were the medicine men who intoned incantations over the patient, danced and made passes over him, or touched him with amulets and other sacred objects Prescribing a witch's brew of herbs came later No one knew what had afflicted him or, if he recovered, what had made him well again

It was not until after man had developed the art of writing that he was able to record his observations of the signs and symptoms of disease These recorded observations led to differentiation among conditions of illness, and what had been simply sickness gradually became specific diseases It is probable that most diseases have existed since the earliest times Their incidence, however, may have varied in considerable degree, some becoming more prevalent and others less

When we speak of a "new" disease as opposed to an "old" one, we mean a disease the knowledge of which has been dis-

covered only recently rather than one which has been recognized for some time as a separate entity It is of interest to note then that the "newest" disease—hyperinsulinism—and one of the "oldest"—hypoinsulinism, or diabetes—are not only curiously related in many ways but also exact medical opposites More than three thousand four hundred years separate our first recorded knowledge of diabetes and that of hyperinsulinism Between them lies almost the entire history of medicine The uncertain and faltering march of that record is well illustrated in the story of diabetes Thus do we set the stage for what is to come

During the latter decades of the nineteenth century the Egyptologists were busy In 1872 at Luxor George Ebers obtained a papyrus written about 1500 B C a millennium before the advent of Hippocrates the Father of Medicine Known as the Papyrus Ebers [1] it has been called "one of the most venerable of medical documents" It gives a number of prescriptions for "medicines to drive away the passing of too much urine" Since the "passing of too much urine is one of the most obvious signs of diabetes it is assumed that the disease was known to the ancient Egyptians even at that early date

Seventeen hundred years later—some five hundred years after Hippocrates descriptions of tuberculosis plague lobar pneumonia and other respiratory diseases—Aretaeus the Cappadocian gave us the first accurate account of diabetes It was Aretaeus who also described tetanus epilepsy the murmur of heart disease and the chest *râles* of asthma Very little is known about this truly remarkable man Probably a native or resident of the hilly country of Asia Minor above the Euphrates valley in the second century he wrote in Greek and his work was lost to us until the middle of the sixteenth century when it was translated into Latin An English translation appeared in the middle of the nineteenth century but

it is only in recent years that Aretaeus' outstanding contribution to the earliest knowledge of diseases has been recognized

Aretaeus not only gave us our first accurate description of diabetes, he also suggested the origin of the name of the disease "The fluid," he wrote, 'uses the patient s body as ladder to escape downward" The Greek word for ladder is *Diabaiton* *Webster's Unabridged Dictionary* derives 'diabetes" through the Latin from the Greek word meaning 't stand with legs apart," as in the position of a ladder

Although Aretaeus knew the signs and symptoms of diabetes, he recognized only the severer forms of the disease and accordingly considered it a rare and fatal malady In common with all other ancient writers, he had no idea of its cause or proper treatment

Fourteen centuries more elapsed before the next step forward was made along the road to a true knowledge of the nature of diabetes While this step appears simple, it took a hardy scientist with a robust nature to make it, and its results were far reaching For it was then that Thomas Willis, the most successful physician of the Restoration, described the sweet taste of diabetic urine [2]

First stimulated by the publication in 1552 of the Latin translation of Aretaeus' work [3] and now greatly augmented by Thomas Willis, investigations of diabetes became a host in *the ensuing years Soon the adjective "mellitus' was added to* the name Derived from the Latin word *mel*, meaning honey, it acknowledged the fact that sweetness had something important to do with this strange disease But still no one had any inkling *why*

During the nineteenth century the incidence of diabetes seemed to increase over that of ancient times More and more cases were observed and studied The relationship to acidosis and the peculiar death in coma became fairly well known But now something happened that has occurred so often in

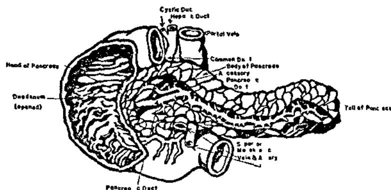
the march of science An epochal discovery was made quite by accident

It was Oskar Minkowski born in Russia in 1858 who brought the story of diabetes into our own times (he died only twenty years ago) In 1889 Minkowski had an argument with his associate von Mering and to settle it they removed the pancreas from a dog to see if the animal could live without it The dog died Other dogs on whom Minkowski repeated the experiment also died And what they died of was identical in every respect to human diabetes Before dying the dogs passed excessive amounts of urine which contained from 5 to 10 per cent sugar *

Now we were getting somewhere at last After three thousand years of observing that diabetics passed excessive amounts of urine—a fact which would logically have led to the belief that the disease had something to do with the kidneys—it was accidentally discovered that the cause must lie in the pancreas

The pancreas is a compound gland from six to eight inches long somewhat resembling a bunch of grapes It is what the gourmet enjoys as sweetbread when it is taken from a calf and served *sauté au beurre noir* The human pancreas lies transversely along the rear wall of the abdomen with its right end or head in contact with the first part of the small intestine and its left end or tail close to the spleen One function of the pancreas is to secrete the fluids that help digest proteins fats and carbohydrates There are two ducts which carry these pancreatic juices into the intestine There are however other digestive ferments in the intestine some derived from the stomach and others from the intestine itself Obviously the digestive process is not entirely dependent upon these pancreatic juices Yet Minkowski's dogs had died when the pancreas was removed Failure to digest food properly then could not be the cause of their deaths—or of diabetes

In 1869 Langerhans a young medical student discovered a



1—*Pancreas and Surrounding Structures*

The head of the pancreas rests in the curve of the duodenum (the first portion of the bowel) The tail extends toward the left The superior mesenteric vein which carries blood from the intestine and the veins from the pancreas stomach and spleen (not shown) empty into the portal vein which carries the blood containing the digestion products and insulin to the liver The pancreatic duct and the common

system

group of cells in the pancreas[5] that were unconnected and apparently unrelated to the rest of the gland These *islands of Langerhans have no ducts with which to transmit any secretion* No one knew what their function was, why they were there

In 1900 however Opie performed an autopsy on a girl who had died in diabetic coma After a careful inspection of all parts of her body, he found the only anatomical abnormality

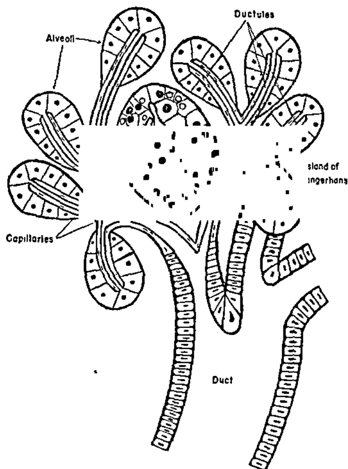
to be a degener...
creas[6] Opie f... , apparent
abnormality r... And so the search narrowed down

Sixteen years later, Sharpey-Schafer suggested that diabetes was due to a lack of some secretion of the islands of Langerhans At that time it was already known that there were a number of organs in various parts of the body with typical glandular structure but without ducts with which to carry their secretions elsewhere These so-called "endocrine," or ductless, glands supply hormones to the body by secreting them into the blood which passes through them The hormones are used throughout the body They therefore have no need to be led to a specific place of local and, consequently, limited application Sharpey-Schafer named the undiscovered hormone from the islands of Langerhans *insulin*

The search had now become a race Nearly every laboratory had at least one person making extracts of pancreases obtained from local abattoirs experimental animals, and autopsy material, in order to obtain the elusive insulin Everyone knew it was there, but no one was able to get a workable extract

In 1892, only three years after Minkowski performed the experiment that set us on the right track at last, Frederick Grant Banting was born in Alliston, Ontario He received his M D degree from the University of Toronto the same year that Sharpey-Schafer suggested his hypothetical hormone, insulin But 1916 was the second year of World War I and Banting enlisted and served with the Canadian army overseas Mankind, especially the diabetic portion of it, is fortunate that he returned safely to his native land He settled to the practice of orthopedic surgery in London, Ontario, in 1920 Orthopedics may seem a far cry from diabetes, but Banting was a determined young man with an idea

He gave up his practice and received permission to use



2—Structure of the Pancreas (Schematic)

The ducts leading from the tiny bulbs (alveoli), whose cells pour their secretion into the central space, join to form progressively larger ducts which finally constitute the two pancreatic ducts The islands of Langerhans are not connected with this duct system These cells manufacture insulin which passes through the walls of the cells and

the laboratory of the University of Toronto to work on his idea A second-year medical student, Charles H Best, was assigned to help him

The idea? Like most great ones it was quite simple, once someone had the imagination to think of it None of the extracts that had been made so far from pancreatic material was successful because the external secretions of the pancreas —those that did not originate in the island [illegible] *being digestant* [illegible] very insulin th [illegible] Best operated on a [illegible] ducts leading from the pancreas to the intestine which normally carry the pancreatic digestive juice The pancreas could not dispose of its secretion, which backed up, producing a degeneration of the pancreatic tissue But it did not injure the island of Langerhans tissue, since it was a separate organ situated within the pancreas The experimental dog did not develop diabetes

After several weeks they removed these degenerated pancreases from this and other experimental dogs and made extracts from them The extracts were then injected into dogs that had been rendered diabetic by removal of their pancreases These dogs were kept alive and in good health for long periods of time They next mixed some of their extract with pancreatic juice This mixture was without effect on experimental diabetics We know now that, like meat, insulin is a protein and is digested by the protein digesting ferments This is why insulin must be injected When given by mouth it is digested like any food, thus being destroyed and of no benefit to the diabetic [1]

Even after Banting's epoch making experiment we were still a long way from the commercial preparation of insulin *If we had to make the extract as Banting did, diabetics would*

the cells of the island, and the bag the limiting membrane. In the illustration the capillaries may be cut directly across to give a round section, while a slanting cut shows a long oval section)

still die in coma because there would not be enough insulin to supply the demand Once the implications of Bantings reasoning were understood, the solution of the problem of preparing insulin from abattoir material was simple The pancreatic juice contains trypsin which is active only in slightly alkaline solutions All that was necessary to prepare insulin from any animal pancreas was to inactivate the trypsin with acid Insulin extracts are made therefore by treating the pancreases with dilute hydrochloric acid The extract is then purified and concentrated, with the various commercial strengths prepared from these potent solutions

Until the discovery of insulin the treatment of diabetes had been simple and ineffectual In view of our present knowledge it is a vivid example of the flounderings of medicine in the pursuit of knowledge

Methods of chemical analysis had developed so that the physician could follow his case with quantitative measurement There are three kinds of food proteins, such as meat, fish, and cheese, carbohydrates, the starchy foods and sweets, and fats We already knew that carbohydrates and proteins would furnish 4 1 calories per gram and fats 9 3 The caloric requirements of the body were also known The body requires just so much protein per day In addition to the energy content of proteins as fuel, they also supply essential elements to repair the wear and tear of living and to build up the tissues of the body The amount of protein we require and the amount that the appetite will demand are fairly well fixed so that adjustments of diet must come in the quantity of carbohydrate and fat we eat

Based upon these facts, the treatment devised for the poor diabetic was to starve him for a few days Some doctors even went so far as to give him "doughnuts" made of talcum powder fried in mineral oil and sweetened with saccharin In other words they let the patient go through the motions of

eating without supplying him with any nourishment This was kept up until his urine was free of sugar Then he was fed gradually increasing amounts of real food until a trace of sugar appeared in his urine The food supply was diminished only enough to remove that trace His physicians now knew his "total carbohydrate tolerance," which was calculated from the protein and fat as well as the carbohydrate in his diet

In digestion all of the carbohydrates are converted into sugar Some 58 per cent of the proteins also are converted into sugar but only 10 per cent of the fats To prevent starvation the body must receive a certain minimum of calories of food energy Since protein is not very variable and since the diabetic can utilize only a limited amount of carbohydrate, energy requirements had to be made up by increasing the intake of fats

Fats are compounds of glycerin [$C_3H_5(OH)_3$] and the fatty acids The latter in combination with alkalies are familiar to us in the form of ordinary soap Acetic acid is a fatty acid common to our daily experience, vinegar, for example, is a 3 per cent solution of acetic acid The simplest fatty acid is formic acid (HCOOH), which we encounter whenever an insect stings us The many fatty acids differ only in the length and complexity of the carbon chain in their make up (*Note* I p 196)

Fats are a useful fuel to be burned in supplying energy for our activities The process of burning is effected by the combination of other elements with oxygen This may occur slowly as in the gradual formation of oxide of iron (rust) on an unused rail exposed to water or moist air It occurs more rapidly when we burn coal or oil in a furnace. The combination is sudden and violent in the explosion of gunpowder or dynamite The process is the same in the controlled explosion of gasoline and air in the internal combustion engine When fats are burned in the body, the process is a slow, step by step

combination of carbon and hydrogen atoms with oxygen These various kinds of burning differ only in their duration (*Note* II, p 197)

The diabetic diets which resulted from increasing the intake of fats were not very palatable But a far worse objection was soon discovered

"Fats burn in the flame of carbohydrate, but in its absence they smoke," was the aphorism in vogue a few years ago Unless glucose—that particular kind of sugar to which the digestive process converts food—is being combusted the body cannot completely burn fats The glycerin part of the fat readily converts into glucose and burns But the remaining fatty acids are incompletely burned, resulting in the production of large amounts of diacetic acid and acetone These appear in the urine where their presence may be detected by chemical tests Diacetic acid is quite strong and is poisonous It breaks down spontaneously to lose carbon dioxide, leaving a residue of acetone (*Note* III, p 198) (Acetone frequently may be found in commercial nail polish removers) Before diacetic acid and acetone appear in the urine, they first suffuse the blood, where the diacetic acid combines with the alkali in the blood, carrying it to the urine This depletes the blood of its alkaline reserve The patient becomes drowsy, then stuporous, if the condition is severe, he goes into a coma and finally dies This process is called acidosis

Acetone is extremely volatile, and some of it will be excreted through the patient's lungs In the days before Banting's discovery, interns in diabetes wards would make their rounds sniffing the breath of patients to detect those who would soon die

In mild cases of acidosis all of the diacetic acid is converted to acetone Since acetone is not acidic, its excretion in the urine does not deplete the body of alkalies But if the urine of an acidotic patient contained diacetic acid in addition to acetone, it was often necessary to inject bicarbonate of soda

into the veins to restore the alkali reserve This condition could be detected by direct chemical examination of the blood, as well as by the presence of diacetic acid in the urine.

Prior to the discovery of insulin, then, all diabetic treatment was directed toward staving off the inevitable end as long as possible In all but the milder forms of the disease the story was always the same Unless the patient died accidentally or from some other disease, such as pneumonia, eventually he arrived at the comatose ending

The liver normally contains a considerable amount of glycogen, the animal starch which it manufactures from the glucose coming from the gastrointestinal tract When we absorb more carbohydrate than we require, the excess, after the liver is saturated with glycogen, is converted into fat and stored in the loose, adipose tissue of the body In the diabetic the paucity of insulin prevents the liver from storing glycogen The space is taken up by fat (The old diabetes wards harbored many patients having large livers with fatty degeneration) This leads to a failure of the liver to handle fats, and often the blood becomes milky from the large content of fat globules suspended in it Some of this fatty or waxy material is *cholesterol*, a substance of prime importance to the body While all its functions are not yet clearly understood we do know that its presence in the bile enables us to digest fats by emulsifying them Cholesterol also is related chemically to vitamin D and to the sex and adrenal hormones, and is believed to be a source for their manufacture

If cholesterol is fed to rabbits[6] the excess will separate out on the walls of the blood vessels and form *atheromatous plaques* These become filled with calcium salts and the animal then has arteriosclerosis (hardening of the arteries) As yet it has not been completely established that the same mechanism causes human arteriosclerosis A report has just been published[7] on research done by Dr John W Gofman and his

s of the Donner Laboratory of Medical Physics at the y of California It indicates that high blood cholesterol is not always a precursor of arteriosclerosis Only when the cholesterol is present in what Dr Gofman has termed "giant molecules, S f 10–20' does the dreaded disease result Long ago, however, it was noticed that when diabetics had an excess of cholesterol in the blood they were extremely prone to the development of arteriosclerosis 'Diabetic gangrene' of the toes was frequently observed in the pre-Banting diabetes wards It was, of course, due to advanced hardening of the arteries and was really arteriosclerotic gangrene The same process of the narrowing of the blood vessels led to what was called "diabetic retinitis," which seriously impaired the patient's vision

The diabetic was prey to other complications of his disease His blood was so rich in sugar that it was an excellent culture medium for bacteria Whenever he had an infection it increased the metabolic demand on his body, making his diabetic condition worse

The bleak prospect of the diabetic has been changed completely by Banting s epochal discovery When insulin became commercially available, the diabetic's chance to live took a sharp upward swing In fact, there was now no reason for an uncomplicated case of diabetes ever to be hospitalized Is it any wonder that Banting's work on his behalf was crowned with the Nobel Prize?

We knew now that diabetes was due to a deficiency of insulin With that life-saving substance available, the treatment was considered quite simple In practice it was not, as we were soon to discover And in thinking it simple we managed to complicate it even more in various erroneous and futile ways *Conditioned by our previous experience,* our minds could not shake off the shackles of the past

The first automobiles were called horseless carriages All

carriages were equipped with buggy-whip holders. Hence, the first automobiles were equipped with buggy whip holders. Q E D. Such is the stubborn inertia of the human mind. It is not surprising then that even after insulin was available and being regularly injected into diabetic patients, we still went through the rigmarole of determining the patient's "carbohydrate tolerance."

We knew that the proportions of carbohydrate and fat should be so regulated that not too much of the latter would be taken. In order to provide enough calories we had to increase the carbohydrate. We knew that 1 unit of insulin would handle 2½ grams of carbohydrate. So we added enough carbohydrate to furnish the required calories and to prevent the incomplete burning of the fat (so that the patient would not go into acidosis) and we covered the carbohydrate in excess of the "tolerance" with insulin at the rate of 1 unit for every 2½ grams. The diet was arranged so that one third of the carbohydrate was consumed at each meal. Efforts were made to keep the insulin intake at a minimum commensurate with keeping the patient alive and reasonably comfortable.

When it comes to food, however, the diabetic is an incorrigible thief. Interns and nurses would discover him prowling the hospital corridors at night trying to beg, borrow, or steal food from other patients. He would encourage his well meaning but unknowing visitors to bring him fruit and even candy. His night table would be searched periodically for the purloined food hidden there.

Despite these handicaps we gravely continued to observe the patient's carbohydrate tolerance. We were so careful! In the hospital's special diet kitchen each dish of food was weighed both before and after the patient's meal to determine exactly how many grams he had eaten. Even if the diabetic had cooperated fully—had followed his diet, had not stolen food—still this weighing of the food would have been a meaningless gesture. It is conceivable, for example, that two

oranges might have approximately the same weight It is equally conceivable however that they might contain completely different amounts of sugar It was senseless to weigh food whose composition could only be guessed But we all did it

In the hospital and clinic the patient s diet would be selected from a number of standard diets He would receive a printed copy of that diet which was the nearest to his individual needs depending upon his weight and the amount of physical activity associated with his occupation (In the office of the diabetes specialist the diabetic could obtain a custom built diet designed for himself alone)

After a few weeks of careful adjustment the patient was presented with his final diet and insulin prescription He was taught to administer his own insulin injections (There was even a portable scale on the market with which the diabetic supposedly weighed his food both at home and when dining out) He was warned to follow instructions and sent home

It was all in vain Having ceased to be dangerous the life of the diabetic had now become complicated Within two or three days all dietary instructions had gone out the window And frequently the diabetic had to return to the hospital It was then that the diabetes specialist decided it would be much simpler to prescribe a single standardized diet rather than one of several select diets since the diabetic invariably would ignore the diet anyway

The sugar that appears in the urine of diabetics is not really a disease process The real *abnormality in diabetes is the* excessive *blood* sugar while urinary sugar is merely an expression of the body s attempt to correct [illegible] abnormality by *ridding itself* of some [illegible] If that [illegible] were not present the blood [illegible] acc [illegible] excessively that the blood wo [illegible] gh the

finer blood vessels Urinary sugar analysis, therefore, essentially is indicative only of the sugar lost in the urine and consequently only of partial value in diabetic treatment A casually passed specimen of urine is not of much significance, diabetes specialists use a sample collected over a twenty-four hour period By analyzing a part of this sample and then multiplying the percentage of sugar by the total volume, a reasonably reliable estimate is obtained of the total amount of lost sugar in a day Some amounts are startling Diabetics have been known to pass more than a pound of sugar in one day

The term commonly used—1 per cent or 2 per cent sugar—*actually is meaningless A 2 per cent sugar urine will drop to* 1 per cent, for example, by the simple expedient of drinking twice as much water The amount of sugar determining the actual severity of the diabetes remains unchanged Only when the excretion is expressed in grams can an accurate judgment be made It is generally considered satisfactory if a diabetic excretes less than 15 grams of sugar per day

One diabetic, who had been under observation at one of New York City's large diabetes clinics for several years, never excreted more than 10 grams of sugar for any day that he was under study One day, however, he happened to have symptoms and signs of a kidney stone and was sent to the kidney clinic, where a urine specimen was analyzed It contained 8 per cent sugar—one hundred times as much as had ever been found in the diabetes clinic over a period of years! The mystery was soon solved For a day or two before reporting to the diabetes clinic, the patient was conscious of his diabetes and consequently watched his diet The rest of the time, however—and it was during one of these periods that he was examined at the kidney clinic—he ate essentially what he pleased Unless, then, reports of diabetes clinics are based upon frequent determinations of the sugar actually in the blood, little reliance can be placed in them The blood sugar

cannot be affected by a short period of "cramming" the proper diet

After a while they stopped putting buggy-whip holders in automobiles So, too, physicians began to question the need for determining the diabetic's carbohydrate tolerance

Assume a patient has a tolerance of 100 grams of carbohydrate At the ratio of 2½ grams of carbohydrate to 1 unit of insulin the patient's own insulin apparatus is supplying about 40 units of insulin a day Thus, if we wish to feed him 200 grams of carbohydrate, he will require an additional 40 units of insulin a day And if we should increase his starch intake to 300 grams, we must give him 80 units of insulin If we give him so much carbohydrate, however, we must cut down on the fats, since the protein requirements are relatively constant

Two Viennese doctors, Adlersberg and Porges conducted just such an experiment [10] To their pleasant surprise their patients were kept in balance with considerably *less* insulin than they had needed when taking only 100 grams of carbohydrate A revolutionary discovery had been made *diabetics are best treated by restricting the fats* Now the doctors as well as the patients discarded the old diets

It was difficult, however, to convince the diabetic of the new concept If sugar appears in the urine we must be taking in too much sugar We must therefore restrict the intake of carbohydrates, since they are entirely converted into sugar This was good logic Logic is that science which deals with the derivation of conclusions from premises according to the laws of valid reasoning What is seldom recognized is that while the *reasoning* might be valid, invalid *premises* lead logically and inexorably to invalid conclusions We must re-examine our premises

Himsworth has shown that diabetics were not excessive eaters of starch before they developed the disease [11] *They were excessive eaters of fats* He has shown that the nations

and peoples whose diet is mostly carbohydrate—Chinese and Japanese whose staple food is rice—little diabetes On the other hand the Jews who much animal fat and the Italians with their large olive oil are most afflicted with the disease[12]

We know now that fat is definitely depressing to the activity of the insulin apparatus The secretion of insulin is stimulated by a rise in blood sugar We therefore actually tend to ameliorate diabetes by withholding fat and furnishing larger amounts of carbohydrate With such a diet the patients are kept in good health by giving them enough insulin to meet their requirements A sensible treatment is to give the patient an outline of about what he should eat The dosage of insulin is slowly increased until the urine is reasonably free from sugar and the blood sugar is at an optimum We are all creatures of habit Once we are accustomed to a diet we will follow it with only occasional minor variations provided that it meets one essential requirement it must satisfy our palates

At first insulin was injected before each meal It had to be The first insulin to appear on the market was an extract of the pancreases of cattle and its action began in about twenty minutes and lasted from four to five hours The diabetic therefore had to take his insulin twenty minutes before each meal so that the peak of its action occurred while the food was being absorbed In the course of time the solutions on the market became better refined and more concentrated so that it became possible to inject the same dose in smaller bulk lessening the discomfort of the injection But the diabetic still had to take an injection at least three times a day Frequently it was necessary to have an extra injection and feeding at bedtime

Even after we had insulin diabetics were quite often brought to the hospital in a coma In such cases the mere administration of insulin was not sufficient to restore consciousness The *normal* blood sugar—that is not during the

fasting or before breakfast state—is about 140 milligrams of sugar per 100 cubic centimeters of blood A severe diabetic might have a blood sugar of 300 mg in the *fasting* state This may appear extremely excessive—more than twice the normal

consumption of 2½ grams of glucose (the form sugar takes in the body), only about 5 units of insulin would deplete the diabetic of this 12 gram excess Since it may take as much as 500 units, or even more, to restore a comatose patient to consciousness, a glucose solution is given intravenously, plus insulin in the ratio of 1 unit to every 2½ grams In order to be in coma the patient must have been neglectful of his condition *for some time, and the injected glucose is* avidly *absorbed* by the liver to restore its depleted stock of glycogen (the substance into which the liver changes glucose for storage)

If the comatose patient has been in acidosis for some time the leakage of alkali induced by the excretion of diacetic acid lowers the alkali reserve Sodium bicarbonate necessary to restore that reserve must be injected—either separately or with the glucose Lactate also may be used for this purpose

At times (but rarely now), the process of alkali depletion has gone so far that irreversible changes have taken place and the patient cannot be roused from his coma He sinks into death despite *the most heroic efforts to save him If we could* get diabetics under control, deaths in coma would practically disappear Much will be said later, in another connection, of the diabetic's sanguine, happy go lucky *temperament that* makes him prone to neglect those things he must do to save his own life

An excess of cholesterol in the blood—one of the dangerous by product complications of diabetes and an indication of the liver's impairment in its function of handling fats—can now be controlled by judicious use of "lipotropic substances"

which improve the liver's ability to metabolize fats terrors of diabetes largely have been removed

In the years immediately following the discovery many efforts were made to prolong its action so that it would no longer be necessary for the patient to take the minimum three injections a day Attempts also were made to prepare insulin by chemical synthesis so that we would not be dependent upon animal sources for our supply In addition a synthetic product is uniform and becomes less expensive than the natural product as production methods are improved The synthetic production of adrenalin already had been accomplished Why should it not be possible to do the same with its fellow hormone insulin?

The first step in the artificial manufacture of any organic substance is its purification for purposes of accurate quantitative analysis so that we may know not only its exact chemical composition but also its chemical structure In order to purify any substance we first must crystallize it The snowflake and the diamond are examples of the purity of the crystalline forms of water and carbon respectively

In 1926 Abel succeeded in preparing insulin crystals [13] But neither he nor anyone else so far has been able to prepare insulin crystals free from zinc or one of several other metals (There is more zinc in the pancreas than in any other organ of the body) Abel's crystalline insulin which has a potency of 22 units per mg has been adopted as the international standard But all efforts to analyze it completely so far have failed We do know that it is of protein nature and of so complicated a structure that it is doubtful if it ever will be made chemically

In 1936 however H C Hagedorn succeeded in producing a form of insulin with a more prolonged action than either ordinary or crystalline insulin He combined the crystalline insulin with *protamine* derived from the sperm of the rainbow trout Protamines are a kind of protein that can precipitate

other proteins from solution. His product, Protamine Zinc-Insulin (universally known as P.Z.I.), was a notable advance.[14] Solutions of ordinary and of crystalline insulin are both somewhat acid. When they are used, the tissue juices pour into the area of injection to neutralize the irritating acid fluid. The insulin is picked up and carried by the blood to wherever it is needed. By adjusting the P.Z.I. solution so that it resembles the blood in being slightly alkaline, the precipitated compound of *insulin acts as a depot whence* insulin is liberated slowly. Instead of occurring in about twenty minutes, as with ordinary and crystalline insulin, the peak of its action occurs as long as twenty-four hours after the injection and its effects are noticeable for some ninety-six hours. By using P.Z.I. the patient could get along with only one injection a day. Hagedorn realized, of course, that his P.Z.I. could not be used in the treatment of coma where a quick response was essential, but he felt it would be excellent for maintaining the good health of the diabetic.

These hopes, however, were *not entirely fulfilled. Despite* the acclaim that P.Z.I. received, it was only another step forward and not the final answer. We sleep during the night and consume food during less than half of each twenty-four hours. It was soon realized that diabetics require their insulin during the early part of the day and not during the night's rest. If the single injection of P.Z.I. were to replace the three or four injections of ordinary insulin effectively, something would have to be done about this time factor. In attempting to solve the problem other substances were combined with insulin. Globin insulin,[15] histone insulin,[16] and *many other* combinations were tried, and some even reached the market. These had time activity periods intermediate between that of regular and protamine zinc insulin. Patients were then treated with two injections in the morning—a small dose of regular insulin to control breakfast and a larger dose of P.Z.I. to take care of the rest of the twenty-four hours. This gave the patient

two needle pricks a day instead of three or four, but by taking them both at the same time, he at least was spared the discomfort and embarrassment of having to carry a hypodermic syringe

Soon it was found that the two kinds of insulin could be combined in the same syringe Since P Z I contains more than enough protamine to combine with all the insulin in it the mixture had to be made with sufficient insulin to combine with the excess protamine and still leave free insulin to achieve the immediate effect desired [17] The amount of insulin added to the P Z I depended upon the experience of the individual doctor Three-to-one and two-to-one mixtures were the most popular Whatever the ratio they were made by simply taking up the two solutions in the same syringe and shaking them together before injection This treatment has now been in use for several years A possibly objectionable feature is the necessity of using two bottles of insulin thus permitting errors in dosage

After a lengthy period of development N P H Insulin was placed on the market in September 1950 [18] Its unabbreviated name is Neutral Protamine Hagedorn Insulin named for Hagedorn who has had most to do with its development and in whose laboratory it was first prepared It is a suspension of tiny crystals and thus a pure substance of definite construction N P H Insulin has its most pronounced action during the first twelve hours, after which its effects taper off for another twenty four hours If administered daily before breakfast therefore there is sufficient overlap to provide insulin at all times while the major part of the substance s activity is concentrated at that time of day at which it is most needed

All physicians with experience in treating diabetics realize that each patient is a law unto himself While N P H insulin is effective in most cases, it does not always work A few patients become ravenously hungry in the afternoon (indicating a fall in blood sugar) and then spill large amounts of

sugar in the morning urine It is futile to try to change their eating habits by shifting the timing of their meals—the patients simply will not cooperate In such cases, we must use one of the other forms of insulin, such as globin insulin or the mixtures described above or, perhaps, multiple doses of unmodified insulin With a little patience and ingenuity, each patient can be controlled with that form of the hormone which proves best for him

Further progress in understanding diabetes can be expected There can be no doubt, for example, that the islands of Langerhans are not alone in producing diabetes A century ago the great Claude Bernard performed an experiment on a number of animals He called it *piqûre diabétique* [19] He punctured the floor of the first ventricle (a space within the brain) and the animal s blood sugar rose, with the excess pouring into the urine This condition, however, was only temporary, and complete recovery followed

Houssay removed the pituitary gland from dogs After they had recovered from the operation, he removed the pancreas In spite of having no pancreas the Houssay dogs did not develop diabetes But when anterior pituitary extract was administered they became diabetic And by injecting very large amounts of anterior pituitary extract into normal dogs they too manifested the increased blood sugar and the urinary sugar discharge of diabetes [20]

Charles H Best, who as a student had assisted Banting, administered large amounts of insulin together with tested pituitary extracts that were known to have been effective in producing diabetes in unprotected animals These insulin-protected dogs did not develop the signs of diabetes [21] Thus, the pituitary, which has been called "the master gland of the body," must have some definite relation to diabetes

When phlorizin is administered to animals, or even to man sugar appears in the urine without any rise in blood sugar [22] This condition must result from an effect on the kidneys, and

it subsides after withdrawal of the drug During the past few years a number of researchers have injected alloxan a substance related chemically to uric acid into animals[25] These animals developed a disease indistinguishable from diabetes and post mortem examinations revealed visible evidence of injury to the islands of Langerhans

What all this may lead to only further research can tell We do not as yet know the precise details of the action of insulin in the body An inkling of one phase of this action is somewhat analogous to that of a candle If we set a match to wax it will not burn But if the wax has a wick we can obtain light from it and the wick is consumed along with the wax This is somewhat similar to the action of insulin with glucose Glucose is needed to furnish energy to every cell in the body It is the fuel of the body Each time you move an arm your muscles burn glucose You also burn glucose in your brain when you think! Insulin is the wick that makes such combustion possible It is essential to the thought and movement which distinguish living matter from inanimate matter

Insulin has another action The body is so constituted that it can function satisfactorily under fairly circumscribed conditions For example the normal temperature of our bodies is 98 6° Fahrenheit This "normal" however is the median of a slight up and-down variation Thus when we arise our temperature is about 98 0° F while for about half an hour after each meal it is 99 0° F If it rises to 100 0° F we have fever and are sick If it falls to 97 5° F we have a chill and are sick Under hot conditions we perspire and the evaporation of the water on our skin cools us off and keeps our temperature normal If we are exposed to cold we shiver and the automatic muscular work done raises the body s temperature to normal

The blood sugar level is also important for the efficient operation of the body Like the body s temperature blood

sugar level fluctuates about a "normal range" Whenever it goes above or below that range, we are sick The normal *blood sugar level supposedly is 80–120 mg per 100 cc of* blood This is not strictly true, however, for that is the normal *fasting* blood sugar level—the level before breakfast, or long *after our last evening meal* But fasting is not a normal state We are not comfortable We are hungry Hence, the normal blood sugar level during the active periods of the day is about 140 *on the same scale* This is similar to the difference in temperature between the 98 0° on arising and 98 6° during the day s activity

The total amount of sugar in the entire blood stream is less than two teaspoonfuls When we eat a meal the products of the digestion of that meal are taken up by the blood If they were taken directly into the general circulation a single two ounce potato would flood the blood with many times as much sugar as it normally contains The blood that leaves the stomach and the intestines, however, carries their products of digestion to the liver Similarly, the blood leaving the islands of Langerhans does not go directly into the general circulation but first to the liver There, under the influence of insulin brought to it from the islands of Langerhans, the glucose (animal sugar) from the products of digestion is converted into glycogen (*animal starch*) *Like ordinary* sugar, glucose is soluble in water, but glycogen is not thus enabling the liver to hold the material within it If this con version did not take place the sugar would be washed right through the liver into the general circulation

The blood that leaves the liver contains the proper amount of sugar *It also carries that portion of the insulin which was* [illegible] This excess in [illegible] enabling [illegible] andle

Let us consider the chain of *events that occur when we eat* some carbohydrate It is digested and converted to glucose,

which passes from the gastrointestinal tract into the blood This blood goes through the liver via the portal vein There being no insulin in this blood the sugar passes unchanged through the liver into the general circulation thus increasing the blood sugar level When the enriched blood now reaches the pancreas the *rise* in blood sugar stimulates the insulin machinery to work Insulin is secreted by the islands of Langerhans into the blood and is carried through the portal vein back to the liver There the subsequent sugar rich portions of blood from the stomach and intestines have the greater part of their glucose filtered out and stored as glycogen The blood now leaving the liver contains the proper amount of sugar

A dam is a barrier between two levels of water Nothing occurs as the higher water level fluctuates unless it reaches the top of the dam The excess water then spills over Similarly if the blood sugar level exceeds its normal—about 140 mg per 100 cc. of blood—and reaches about 165 it spills over into the urine This action occurs if the kidneys are normal Sometimes however the kidneys "renal threshold is low and sugar will appear in the urine despite normal levels in the blood This condition known as *renal diabetes* is quite harmless On the other hand severely damaged kidneys may fail to pass any sugar in spite of very high levels in the blood Persons with that combination have diabetes without ever actually showing any trace of sugar in the urine Sugar in the urine then merely represents an economic waste It is the result of a compensatory attempt by the kidneys to correct an unnatural situation—overrich blood

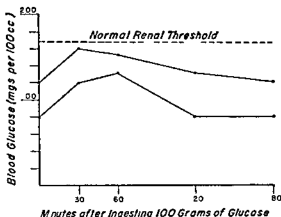
In the vast majority of cases in which diabetes is suspected the suspicion can be confirmed or denied by a simple test of the urine passed about two hours after a meal If the meal has included considerable amounts of starchy foods the presence or absence of sugar in the specimen will be highly indicative of the existence or absence of diabetes

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The blood that leaves the liver contains the proper amount of sugar It also carries that portion of the insulin which was not required to convert glucose into glycogen This excess insulin circulates with the blood throughout the body, enabling each cell to utilize the glucose It is the wick in the candle

Let us consider the chain of events that occur when we eat some carbohydrate It is digested and converted to glucose,



3—*Tl e Glucose Tolerance Test*

[illegible]

sults Our know ledge had not been sufficiently advanced to account for *low* alues The dotted line ind cates the normal renal threshold When the blood sugar rises above th s value the excess sugar sp lls over into the ur ne in an attempt by the kidneys to restore the blood sugar to its optimum value

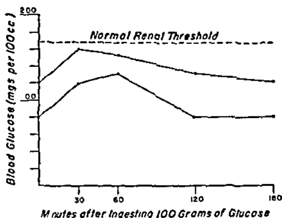
The Glucose Tolerance Test may be influenced by the pa ent s previous eating [24] If he has been taking large amounts f fatty foods the tolerance will tend to be low—the blood ugar level will tend to be higher If he has been eating more f the carbohydrate foods however his tolerance will tend

nce Test the fasting blood sugar is taken after which the patient drinks only 50 grams of glucose in solution Thirty minutes later his blood is drawn again, and another 50 gram glucose solution is administered A third blood sample is

If the specimen contains but a small amount of sugar, the case may be *renal diabetes* This is the entirely harmless con dition in which the level at which sugar filters into the urine is abnormally low If, on the other hand, the specimen is sugar free and the patient nevertheless has such usual symptoms of diabetes as excessive urine and thirst because of the great *loss of water, then the condition may be diabetes insipidus* This entirely different illness is due to disease of the pituitary gland within the brain Another condition sometimes occurs in women toward the end of pregnancy, or during the nursing period, in which they excrete lactose (milk sugar) Again, there is a perfectly innocuous condition called *pentosuria,* wherein sugars called pentoses" (containing five carbon atoms instead of the six of glucose) are found in the urine *Occasionally this will occur in otherwise normal people who* have eaten such fruits as apples and plums which contain significant amounts of pentoses Pentosuria is without signifi cance insofar as an individual s health is concerned

In all cases in which there is the slightest doubt, the Glucose Tolerance Test will give the doctor the right answer There are several modifications of this test in vogue The simplest and the one used most extensively consists in taking *a sample of the blood in the fasting state, before breakfast* The patient then drinks 100 grams of glucose dissolved in water, flavored with lemon juice Blood and urine samples are taken at half hour intervals for two hours The results are plotted on a graph similar to the one on the next page

In the case of a healthy person, all the urine specimens should be sugar free The initial blood sugar level should be between 80 and 120 mg per 100 cc of blood The level should *rise to not more than 160 in thirty or sixty minutes,* and it should return to its initial value within two hours If these conditions are not met, the patient has diabetes The severity of his case may be judged to some extent by the height to which the blood sugar level rises

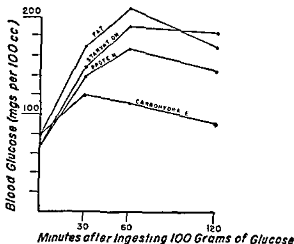


3—*The Glucose Tolerance Test*

even lower but no explanation was at hand for these paradoxical results Our knowledge had not been sufficiently advanced to account for low values The dotted l ne indicates tl e normal renal threshold When the blood sugar rises above this value the excess sugar spills over into the urine in an attempt by the kidneys to restore the blood sugar to its optimum value

The Glucose Tolerance Test may be influenced by the patient s previous eating [24] If he has been taking large amounts of fatty foods, the tolerance will tend to be low—the blood sugar level will tend to be higher If he has been eating more of the carbohydrate foods, however, his tolerance will tend to be higher—the rise in blood sugar level will not be so great

Because of this variable, the Exton Rose Test is being used more extensively [25] In this modification of the Glucose Tolerance Test, the fasting blood sugar is taken, after which the patient drinks only 50 grams of glucose in solution Thirty minutes later his blood is drawn again and another 50 gram glucose solution is administered A third blood sample is



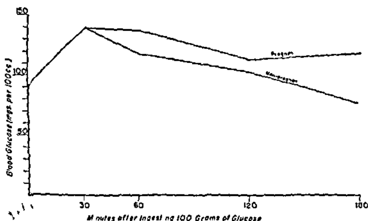
4—Effect of Diet on the Glucose Tolerance Test

This chart shows the effect of an earlier meal on the Glucose Tolerance Test The level of blood sugar depends on the supply of sugar coming from the stomach and its removal by the liver under the influence of insulin Carbohydrate stimulates the production of insulin while fat depresses that process Protein feeding has an effect similar to that of carbohydrate since 56 per cent of protein is converted into glucose during digestion but this effect as is to be expected, is less than that of the direct feeding of straight carbohydrates In starvation the stored body fats are consumed as food the effect would be similar to that of fat feeding but to a lesser degree

taken after another thirty minutes This test is not significantly influenced by any previous dietary habits Normally, the fasting blood sugar lies between 80 and 120 mg per 100 cc of blood The blood taken half an hour later should not be more than 75 milligrams richer in sugar The third blood sample should not be more than 5 milligrams higher than the second The urine samples should all be sugar free This test is easier on both patient and laboratory, since only three blood samples are required instead of five

The stimulus to the patient s islands of Langerhans that makes them secrete insulin is a rise in blood sugar [26] In the Exton-Rose Test the first dose of glucose causes the patient's

insulin apparatus to produce some of the hormone When the second portion of sugar is given, there is so much insulin available that the blood sugar should not rise much In some cases it even falls In diabetes, however, the insulin apparatus is so sluggish that not enough insulin is secreted to prevent the second dose of glucose from raising the blood sugar level



5—*Effect of Pregnancy on the Glucose Tolerance Curve*

The upper curve indicates the average findings in fifty one pregnant women the lower the average of 300 nonpregnant women None of either group was diabetic

The glucose tolerance curve also is affected by pregnancy While the first part of the curve is not changed significantly, the rise is prolonged [27] We shall have occasion to refer to this fact later

In normal, healthy operation, the various parts of the body expend the sugar which the blood supplies to them The blood sugar level then falls, and this drop stimulates the secretions of the adrenal cortex These substances (cortisone, cortin, etc) induce an action antithetical to that of insulin Carried to the liver by the blood, they there effect the re-

conversion of stored glycogen to glucose It is the balance be tween insulin and the adrenal cortical hormones then which keeps the blood sugar between the normal levels to which the body s functions are adapted

The medulla the inner portion of the adrenal glands secretes adrenalin which also induces an action antagonistic to that of insulin Like the cortical hormones of the same glands it causes the liver to convert glycogen back to glucose Unlike the cortical hormones however, adrenalin is not used in the moment to moment operation of the body Adrenalin acts suddenly and in spurts It is an emergency hormone called upon when there is a great demand for energy It pre pares the animal for fight or flight when its muscles re quire large amounts of fuel Adrenalin also quickens the pulse rate so that more blood is pumped to all parts of the body It raises the blood pressure so that the muscles are flooded with blood containing more fuel for the emergency

The liver is unique among organs in that it has a double blood supply Not only does it receive the discharged blood from the digestive tract pancreas and spleen through the portal vein but it is also connected with the general circula tion by the hepatic artery The cortical hormones get to the liver through the hepatic artery since the veins leaving the adrenal glands are not connected with the portal vein but with the general venous system

The liver is not the only storage for glycogen This func tion is shared with the muscles The changes from glucose to glycogen and back again take place in the muscles just as they do in the liver and under the same circumstances and stimuli But most of this action occurs in the liver

Compare the operation of the human body to that of an automobile Let the gasoline tank represent the liver the carburetor the insulin apparatus When we eat we fill our liver with body fuel—sugar converted into glycogen We now are able to drive our body for several hours without refuel

ing while our insulin apparatus regulates the proper mixture—maintains the proper blood sugar level

Should the insulin supply be inadequate however the liver cannot effectively convert sugar to glycogen Too much sugar is then washed into the blood stream The blood sugar level rises and remains high This is diabetes Thanks to Dr Banting the diabetic s insulin deficiency can be made up with insulin from the pancreas of a deceased cow But without injections of insulin—like the automobile that has been choked too much—the diabetic body is trying to run on too rich a mixture

There is an opposite condition in both cars and people The mixture may be too *weak* The blood sugar level remains too *low* because the body s islands of Langerhans supply the liver with too *much* insulin This is hyperinsulinism

Hyperinsulinism was discovered two years after Banting had solved the diabetic s major problem We know now that there are many more sufferers from this newest disease or condition than there are diabetics The discovery of hyperinsulinism opened one more tightly closed door Through it there blazes new light into the dark corners of our ignorance of many things This new awareness its significance and its hope are the subject matter of the remainder of this book

3

—And the New: Hyperinsulinism

"MEN IN WHITE"—INSULIN SHOCK *vs* DIABETIC COMA—SEALE HARRIS—THE SIX-HOUR GLUCOSE TOLERANCE TEST—THE FOUR CONDITIONS OF HYPERINSULINISM—"THE STEPCHILD OF MEDICINE"—HYPERINSULINISM'S DISGUISES—CAFFEINE—TREATMENT THE HYPERINSULINISM DIET

IN THE children's ward of a big city hospital the beds are screened off from each other, giving a meager degree of privacy to each patient Behind one such screen a little girl of ten lies back with eyes closed Her skin is pale and clammy She is a diabetic and she has suddenly lost consciousness Her distracted parents stand beside the bed A student nurse is speaking rapidly on the telephone

'South 210, calling Dr Ferguson At once!

The mother is frightened by her child s ghastly pallor The ... in particu ... Why isn't he here

Presently Dr Cunningham comes in He is a dignified and impressive-looking gentleman He wears a goatee, a pince nez, and has a throaty voice He is just a bit too much of the

professional He belongs to a vanishing species, much rarer today than it used to be

"What's happened here?" he asks Barbara, the young student nurse

She tells him crisply, "Complete collapse About two minutes ago"

Dr Cunningham asks to see the chart, which she hands him With pompous deliberation he looks at it, frowns, shakes his head, and remarks, "H'm This is bad!' He picks up the child's wrist to take her pulse He closes his eyes

Barbara starts to tell him, "Pulse is barely—" but he silences her

"Let me have my stethoscope," Dr Cunningham tells Barbara He takes the instrument and listens to the child's heart Then he announces, 'Diabetic coma"

The child's parents are so upset that Dr Cunningham banishes them to the hall outside the ward He then has the young student nurse prepare 40 units of insulin and 50 grams of glucose for an immediate injection

After our discussion of the coma of acidosis, it is probable that you agree with Dr Cunningham's diagnosis, that little Dorothy Smith has gone into a coma from which she can be revived only by a prompt injection of insulin If so, you are just as mistaken as Dr Cunningham The little girl has not sunk into the coma of diabetic acidosis She has collapsed suddenly into the stupor of insulin shock Additional insulin will probably kill little Dorothy Smith whose parents wait in anguish out in the hall

Barbara is dimly aware of this, and when ordered to prepare the insulin injection, she protests, "But, sir, Dr Ferguson advised against insulin"

As Dr. Ferguson is only the hospital intern, while Cunningham is the family physician, this strikes Cunningham as a piece of impertinence of which only a student nurse

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—And the New: Hyperinsulinism

"MEN IN WHITE"—INSULIN SHOCK *vs* DIABETIC COMA—SEALE HARRIS—THE SIX-HOUR GLUCOSE TOLERANCE TEST—THE FOUR CONDITIONS OF HYPERINSULINISM—"THE STEPCHILD OF MEDICINE"—HYPERINSULINISM'S DISGUISES—CAFFEINE—TREATMENT THE HYPERINSULINISM DIET

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'South 210, calling Dr Ferguson At once!"

The mother is frightened by her child's ghastly pallor The father paces about, nervously demanding of no one in particular, 'Where is Cunningham?' the family physician 'Why isn't he here?'

Presently Dr Cunningham comes in He is a dignified and impressive looking gentleman He wears a goatee, a pince-nez, and has a throaty voice *He is just a bit too much of the*

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As Dr Ferguson is only the hospital intern, while Cunningham is the family physician, this strikes Cunningham as a piece of impertinence of which only a student nurse

could be guilty Indignantly he exclaims, 'Ferguson? You'll please take your orders from me "

Fortunately for the patient, Ferguson comes in at this moment He looks at the child and remarks, "I was afraid of shock ' An argument follows in which the young intern tries hard to be respectful to the older man who outranks him in the hierarchy of medicine 'I beg your pardon, Doctor, but isn t insulin contraindicated here?"

"No It s our last chance," says Cunningham stubbornly

Aware of the young life that ebbs away with each passing second, Ferguson persists, "Doctor, I mean no offense, but I've studied this case history, and it looks like shock, not coma" Cunningham denies it "But the clinical picture is so clear cut Ferguson goes on, urgency creeping into his voice 'Look at the patient She's pale, cold, clammy Temperature subnormal She s complained of hunger Sudden onset"

Cunningham is annoyed 'Suppose you let me handle the case, young man' He directs the nurse to prepare the child s arm for the injection She does so

With helpless despair Ferguson watches Cunningham take up the loaded syringe Ferguson knows it is loaded with death, a murder weapon He places his hand on Cunning ham's arm and pleads with him, "Please, Doctor! Call one of the other men Ask them anybody"

"There is no time, Cunningham says coldly "Take your hand off," he orders, his urbanity cracking a little

'That insulin is going to prove fatal," says Ferguson

"Get out of here, will you? I don't want any interruption" Cunningham is getting angry now

Then, like so many young people who have defied a superior to save a life or gain some equally vital victory, Fer guson makes that split second decision Without conscious heroism he risks his career by taking the insulin loaded syringe from Cunningham's hand and squirting its contents on the floor

Cunningham sputters with outraged indignation "Why did you do that you fool?"

Ferguson ignores him He has taken command It is as if the older man were no longer in the room With cool efficiency the young intern proceeds with what he knows must be done with all possible speed He is giving a preview of the sort of doctor he is to be He will grow with his times not stagnate as Cunningham has stagnated He will never take himself more seriously than the situation that happens to confront him

"Nurse shock position" Ferguson commands Barbara moves quickly and raises the foot of the bed Ferguson looks out from behind the screen and calls out to another nurse Sterile glucose quick and a 30-cc syringe" Barbara tells him that she has glucose ready 50 grams of it Half of that will do he tells her Then to the other nurse he calls "Never mind the glucose A hypo of adrenalin And some hot packs and blankets"

By now Cunningham has sufficiently recovered from the shock of having a mere intern brush him aside to fulminate "What do you think you're doing? I'll have you brought up before the medical board I'll have you thrown out of this hospital"

All right" says Ferguson "Have me thrown out I don't give a damn! And he doesn't He is busy saving a life He goes right ahead After the nurse has swabbed the patient's arm with alcohol he injects the glucose and then the adrenalin He and the nurse apply the hot packs and cover the little girl with blankets

All the while Cunningham is fuming You'll pay for this young man The patient's life is in your hands"

Ferguson doesn't seem to have heard "That's about all we can do" he tells Barbara

"You report downstairs at once!" Cunningham orders But Ferguson and Barbara stand strained tense watching the

patient After a long moment the little girl raises her hand to her forehead and opens her eyes She looks at Ferguson who leans toward her Very faintly she says, 'Dr George, I'm thirsty"

The battle is won A life is saved

This scene actually took place, only on the stage of a theater We have transcribed it from Sidney Kingsley's fine play, *Men in White*,* in which he so skillfully probed the anatomy of the medical profession

During the twenty eight years that insulin has been used in the treatment of diabetes, many patients have suffered occasional insulin shocks Some of them have died of shock. This condition would come about when an overdose of insulin was given or when a meal was unduly delayed Another cause of insulin shock was exercise It was said that a game of tennis or golf was equivalent, in effect, to 15 units of insulin By quickening the metabolic processes of the body, exercise enables the patient to get along with less insulin Trouble arises when the diabetic takes his insulin and then indulges in some activity for which he has made no provision by subtracting some insulin from his usual quota

When the medical profession was first wrestling with the
es would
was pre-
error, or
because the patient did something, such as [illegible], which reduced the need, or again because the patient's improvement made his requirements smaller The subsequent drop in blood sugar instituted by the insulin progressed too far The re sultant physical condition is known as insulin shock

The pa-
[illegible]tion of
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iptoms

* *Copyright* 1933, by Sidney Kingsley

(A *symptom* is experienced by the patient and described to the physician, a *sign* is observed by the doctor himself A headache, for example, is a symptom, while a rash is an obvious sign) As the signs of insulin shock become evident, the patient begins to tremble, his gait is unsteady Some victims exhibit a *muttering delirium* (*At times they have been picked* up by police for alleged drunkenness) In spite of feeling famished, a patient occasionally will be assailed with nausea and vomit the food he has taken to relieve his hunger Eventually the victim of insulin shock goes into a deep stupor Some patients have convulsions in the midst of their stupor

The deep stupor of insulin shock—to the confusion of *Men in White's Dr Cunningham and others—looks exactly like* the coma of diabetic acidosis Both are states of unconsciousness To some, 'stupor' may indicate a state of unconsciousness a shade less profound than coma," or again the words may be used properly as synonymous In medical usage, however, the two words are not the same Though stupor and coma describe conditions identical in appearance, their cause is different The American Diabetes Association has recommended calling the unconsciousness of insulin shock *stupor*, reserving the term *coma* for that of diabetic acidosis This avoids confusion There is only one physical sign to differentiate between the two in coma the eyeballs tend to be *soft*, in stupor, they do not In addition, of course, the odor of acetone cannot be detected on the breath in stupor

In most cases there was little difficulty in making the diagnosis If the patient had been under treatment in the hospital it was quite simple Coma usually comes on gradually, while insulin shock strikes with lightning like rapidity When an unconscious patient was brought to a hospital, however, considerable laboratory work often was required to determine which condition was present A low blood sugar ostensibly *indicated stupor It was entirely possible, however (and it* actually did happen), that, as the result of an overzealous

problem changed its complexion At first it was serious and baffling Frequently diabetes specialists would be called early in the morning to see a patient who had been switched re cently from insulin to Protamine Zinc-Insulin The patient would be found in the stupor of insulin shock A sterile glucose solution would be injected intravenously the patient would revive almost immediately and the doctor would leave Within almost a matter of minutes the patient would be in shock again The doctor would have to return and administer another injection of glucose What had happened was soon understood *Protamine-Zinc-Insulin has its peak action about* twenty four hours after the injection The first shock coincided with this peak The first glucose injection took care of only that insulin which was circulating in the patient s blood at that time But there was still a depot of unused insulin at the site of the previous day s P Z I injection When more of this residual insulin was absorbed the blood sugar again fell In order to prevent a repetition of this process sweet drinks would be administered for a number of hours At times it was *necessary to administer sterile glucose intravenously by a slow* drip lasting for as long as twenty four hours This was neces sary for example in the case of a patient who inadvertently bought a bottle of P Z I twice as strong as had been pre scribed

Today such accidents are rare We have learned that it is safer to undertreat rather than risk overdosage We now at tempt to keep the blood sugar as nearly normal *as possible We* have learned to be not quite so concerned by some sugar in *the urine Our aim is to keep it* down to 15 grams (half an ounce) a day But even properly administered P Z I may sometimes produce a slight insulin reaction with very mild symptoms In such cases the patient may be a bit tired or have a headache on awakening but this disappears soon after he has eaten breakfast In addition he may be fatigued be fore other meals

—AND THE NEW HYPERINSULINISM

We have dwelt at some length on insulin shock because its symptoms are important to the rest of our story

In 1924, only one year after insulin was in general use, Dr Seale Harris, then professor of medicine at the University of Alabama, noticed that many people who were not diabetic and who were not taking insulin nevertheless experienced some of the symptoms of insulin shock

Seale Harris knew that other ductless glands can be over or underactive Diseases resulting from abnormalities of the thyroid gland, for example, were known centuries before we had any knowledge of ductless glands as such, or of their functions Something has been known about Graves' Disease (toxic goiter) since early in the nineteenth century This we now know to be *hyper*thyroidism Its victims have a rapid pulse and elevated blood pressure they lose weight and are extremely nervous In the sixteenth century, Paracelsus wrote about *myxedema* Myxedema (cretinism in children) is *hypo*thyroidism and is characterized by a slow pulse, low blood pressure obesity, and a phlegmatic disposition border-

litus was just such an aberration It was *hypo*insulinism Harris investigated those nondiabetics who had symptoms of insulin shock and found their blood sugar level to be abnormally low He further found that if their blood sugar level dropped abruptly these patients were prone to a more extreme attack of the symptoms of insulin shock

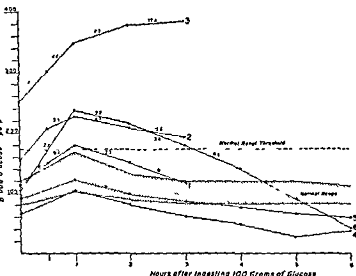
Seale Harris reported on this matter in September, 1924,[1] and called the condition *hyper*insulinism He maintained that it resulted from an excessive secretion of the hormone by the

diabetes [2] This consisted of prolonging to six hours the period

during which the blood is analyzed for sugar and drawing the blood samples at hourly intervals Harris noticed that all his hyperinsulinism patients showed drops of sugar concentration as the analysis time was lengthened Such a drop does not occur in the normal body

By means of this six-hour test, Harris was able to verify another startling observation In certain diabetics the symptoms alternated between those of diabetes and those of spontaneous insulin shock When given to these patients, the six hour Glucose Tolerance Test revealed curves which for the first three hours were similar to those of any other diabetic After that, however, the sugar level took a sharp dip to the levels indicating hyperinsulinism If these patients were tested in the standard manner there was nothing in the results to indicate that they were not pure diabetics But the new six hour test dramatically drew attention to a hitherto unknown condition, for which Harris coined the term *dys*insulinism To explain this strange condition which partakes of the nature of two exactly opposite conditions, Harris postulated a time delay in the secretion of insulin in response to a metabolic demand, followed by an overcompensation which floods the blood with an excess of insulin Insulin secretion is roughly analogous to rainfall The normal person's insulin secretion is like the normal rainfall of the temperate zone Just as rain occurs in moderate amounts every few days, so insulin is secreted at frequent intervals in response to the metabolic demand and no more The diabetic is a desert dweller Like the desert s rainfall, the secretion of insulin is insufficient for life Hyperinsulinism, on the other hand, is the continuous downpour in a region of endlessly soaking rains *Dysinsulinism* is the parched desert pining for rain and getting it from time to time in a torrential flood that does much harm and no good

While *hyperglycemia* (literally *too much sugar* in the blood) may result from other causes, diabetes always produces



6—*The Six hour Glucose Tolerance Test*

For comparison actual cases involving the shorter test have been included to demonstrate diabetic curves The small figures above the

amounts of sweets

2 A moderately severe case of diabetes This patient must take insulin

3 An extremely severe diabetic This sometimes is called 'total diabetes" for the patient has practically no insulin of his own The rise in blood sugar persists for several hours This patient requires more than 100 units of insulin a day

4 Manifest hyperinsulinism This patient had the classical symptoms of hyperinsulinism She "blacked out" on many occasions It will be noticed that the level at the sixth hour is higher than at the fifth This rise probably is due to stimulation of the adrenal glands by the great drop in blood sugar, after which the adrenal hormones begin to raise that level

an excess of blood sugar. Similarly, *hypoglycemia (too little sugar)* may result from conditions other than hyperinsulinism, but hyperinsulinism always produces a deficiency in blood sugar.

In 1926 Gray and Feemster reported the case of a diabetic woman who gave birth to an apparently normal child.[3] The infant soon died in insulin shock. The fetus had developed in an environment that was hyperglycemic—overrich in blood sugar. While there is no direct connection between the maternal and fetal blood vessels, the sugar in a pregnant woman's blood diffuses freely into the fetus' blood. To compensate for this, the cells in the islands of Langerhans of the developing fetus multiplied in excess of what would have been normal, had its prenatal environment been normal. The result was that when the child was born and its connection with the mother's overrich blood sugar level severed, too much insulin was secreted and the baby died of severe insulin shock.

Diabetic mothers greatly tend to abort before term. The babies usually are quite large, but modern practice avoids this complication by delivering the babies prematurely. There may be other complications, however, as a result of frequent disturbances of the sex hormones in diabetics. This condition sometimes causes the development of congenital defects in the child, such as missing digits, webbed fingers, or club feet.

In 1927, at the Mayo Clinic in Rochester, Minnesota Doctors Wilder, Allen, Power, and Robertson reported a case that has since become famous.[4] The patient was a physician, not diabetic, who had many attacks of insulin shock. These came on with increasing frequency and severity. He had to be given increasing sugar at increasingly frequent intervals. He had to be watched in his sleep and awakened when he twitched, so that he could replenish his blood sugar. Although

the test how-

his case was studied thoroughly, nothing could be done for him and he died An autopsy revealed a hitherto unknown condition a malignant tumor—a cancer—of the islands of Langerhans These diseased cells had thrown off secondary growths which, having traveled through the lymph or blood, had taken root in other organs of the body (This process is known medically as *metastasis* A metastasis from a malignancy has the nature of the parent growth) When these secondary growths were extracted with acidulated water and the extract was injected into rabbits, the animals went into insulin shock and there was a great lowering of their blood sugar levels The patient had suffered from a newly discovered type of cancer—insuloma He had been manufacturing insulin all over his body

The case was *important for several reasons* It had revealed *a new type of cancer* It had established one cause of hyperinsulinism—a malignant tumor of the islands of Langerhans in the pancreas And it had shown that insulin could be secreted in other parts of the body than the pancreas The case helped Seale Harris in reasoning about the problems of hyperinsulinism There were many points of similarity between the case at the Mayo Clinic and those he had seen in Birmingham They differed only in severity and in the fatal outcome of the Rochester case

In 1929 Graham operated to remove a tumor of the islands of Langerhans which differed from the latter case in that it was not malignant This growth did not expel small portions to travel in the body fluids[a] Allen O Whipple has thoroughly investigated these benign tumors of the islands of the pancreas He has operated on many patients afflicted with them and has reported many cures Whipple and others have also described a similar condition in which, while there is no *tumor or group of tumors in the pancreas*, there is a generalized diffused enlargement of the islands of Langerhans By removing a part of the left end or tail of the pancreas—

the region in which the islands are generally most numerous —the patient can be restored to health [6]

Thus we have four similar conditions of hyperinsulinism differing in cause, severity, and treatment necessary to effect a cure The severest and, fortunately, by far the rarest form of hyperinsulinism is that caused by malignant insuloma Treatment is ineffectual as in many types of visceral cancer, mortality is 100 per cent The second variety is caused by a *benign and removable tumor of the islands of Langerhans* One or two lumps grow in the pancreas and these secrete too much insulin (Sometimes they can be felt through the abdominal wall At operation if on the surface of the pancreas the tumors can be seen as lilac-colored lumps of from 1 to 2 centimeters in diameter and partly protruding from the surface of the gland When they are deeper they can be felt through the softer tissue of the normal portions of the gland in which they are imbedded) These tumors can be removed by surgery Whipple requires that three conditions be present in the patient before he will operate the fasting blood sugar must be below 50 mg per 100 cc of blood, the frequent attacks must be accompanied by an extremely low blood sugar level, the attacks must be completely relieved by administration of glucose, with the blood sugar level rising as the symptoms subside Under these conditions Whipple not only indicates that he favors operation but seems to consider it essential to prevent the benign tumors from becoming malignant or causing mental deterioration as a result of keeping the brain tissue undernourished (On June 11, 1951, Dr Whipple received the American Medical Association's distinguished service award for his work)

The third kind of hyperinsulinism is that due to a generalized enlargement of the island tissue without any concentration into any demonstrable lump This type can be cured by the removal of part of the pancreas It should, however, be given medical care for some time before operation,

since many such cases have yielded to nonsurgical treatment

The fourth and by far the most common form of hyperinsulinism is the one that Harris called "functional hyperinsulinism" In functional hyperinsulinism there apparently is no demonstrable anatomical change in the islands of Langerhans in size structure or number at least as far as present methods of investigation reveal But these apparently normal glands nevertheless produce more insulin than they should Harris found this fourth type of hyperinsulinism to be even more prevalent in his experience than its opposite diabetes He devised a diet to overcome this condition [7]

First indicated in 1924 and reported on again in 1932 and 1936 Seale Harris great discovery is still only vaguely known to most rank and file practitioners According to Dr Martin Grotjahn eminent Los Angeles psychiatrist it has been the Stepchild of Medicine To this day many prominent investigators challenge the Harris findings and conclusions or ignore them This in spite of the fact that by the most conservative estimate there are well over a million persons suffering from hyperinsulinism in the United States and probably from ten to thirty times that number These are the wretched people who usually are treated ineffectually for everything under the sun except the condition that afflicts them Persons who at last were found to be suffering from hyperinsulinism have been treated for coronary thrombosis and other heart ailments brain tumor epilepsy gall bladder disease appendicitis hysteria and every sort of neurosis They have been told repeatedly that their trouble is all in the mind" and sent to the psychoanalyst

Some of the eminent surgeons who deny or doubt the existence of functional hyperinsulinism nevertheless have been forced to admit that they have operated on a patient (who had exhibited all the signs and symptoms of hyperinsulinism) to perform their pancreatotomy, and found neither a tumor to remove nor any hypertrophy or other anatomical

indication that there was anything the matter with the patient's islands of Langerhans! This has happened not once but several times As a result, it has been suggested that perhaps in such cases the tumor is too small to be seen!

The normal conservatism of the medical profession, the "cultural lag," the inability of the hard pressed present day practitioner to keep up with the literature—a condition made more acute than ever by the demands on his services during World War II, which came at the very time when Harris' findings would have been absorbed under peacetime conditions—all these considerations help to explain the stepchild treatment of hyperinsulinism But they do not altogether suffice The best explanation of the anomaly is found in a letter from Dr Sidney A Portis of the University of Illinois who has made important contributions to the knowledge of hyperinsulinism (which will be discussed in a later chapter) Dr Portis suggests that the trouble with hyperinsulinism is that *it cannot be packaged, publicized, and sold over the counter* in a drugstore The 'miracle drugs,' starting with insulin itself, have caught the imagination of the public They are something tangible which can be obtained in a bottle, and the public's reaction to them has in turn affected the physicians attitude There is no glamorous cure for hyperinsulinism that can be bought in a package Its diagnosis and treatment demand pains from the physician and sacrifices from the patient who must give up candy, sugar, pies, alcohol, coffee and sometimes smoking Being human, doctors much prefer to write a prescription for a miracle drug than to order the execution of habits of self indulgence hitherto considered quite harmless

In the end, however, fate has been kinder to Dr Harris than to many other trail blazers In 1949 the American Medical Association gave Harris an "achievement award" and caused a medal to be struck in his honor This signal distinction has been made only a dozen times in the association's century of

existence As the far reaching consequences of his discovery spread throughout the medical profession and lead to further discoveries and greater understanding it is to be hoped that other honors and rewards may come to Seale Harris

Harris called hyperinsulinism the "hunger disease" Others have called it "fatigue" and "chronic fatigue" Hunger, of a most ravenous kind, is certainly the outstanding symptom while fatigue is undoubtedly a common symptom in many cases Admittedly hyperinsulinism is a mouthful. Hypoinsulinism has an easily spoken name in diabetes Perhaps, hyperinsulinism will in time be known as sugar starvation, for that is what it literally is Sugar is the fuel of every cell in the body While most body cells can derive some nourishment from other sources, however, the nourishment of the brain is exclusively glucose Moreover, unlike some other organs which store sugar the brain is dependent upon the moment to-moment blood sugar level for its functioning Blood sugar, then, is as important to life as the air we breathe, it is sugar which burns in the oxygen we breathe

Before discussing the signs and symptoms and treatment of hyperinsulinism, however, we must understand how it comes about

The stimulus to the islands of Langerhans which causes them to pour their secretion into the blood is a rise in blood sugar It is not the actual level, no matter how high, but the jump in that level A rise from 80 to 140, for example, has about the same effect as one from 180 to 240 (This effect is well known It is the basis for the Exton Rose sugar tolerance test) When we eat the processes of digestion convert the food into glucose at the rate of 100 per cent of the carbohydrates, 56 per cent of the proteins, and 10 per cent of the fats The blood carries the glucose from the intestinal tract into the liver, but there is little insulin in the liver at the time The sugar passes through the organ largely unchanged and is carried by the

which records the "brain waves" and from which we can now diagnose and even localize brain tumors and other conditions within the skull.) A competent brain specialist diagnosed this woman's condition as a possible brain tumor, and preparations were made for an exploratory operation. Fortunately, however, a Glucose Tolerance Test was given first and the correct diagnosis of hyperinsulinism was clearly revealed. The operation was not performed, and the patient has been in good health ever since the proper treatment was instituted.

The attacks tend to occur if a meal is delayed or if any undue exertion depletes the store of sugar in the blood. Sometimes they will occur after an illness which subjects the body to unusually great wear. A salesman who traveled about the city in his car had been ill with grippe. Because he had not called on his customers for several weeks, he now rushed about to get in as many calls as possible. One day he went without luncheon. At about four in the afternoon he felt dizzy and pulled over to the curb and parked his car. It was fortunate that he stopped, because he suddenly slumped over the wheel. The usual crowd gathered. A call was put in for an ambulance, but the man revived before it arrived. (This incident occurred early in the postwar years before hospitals had resumed their prewar practice of having an intern ride in every ambulance.) Urged by the ambulance attendant, the man drove to the hospital where an intern made a diagnosis of coronary heart disease. This was not confirmed by the electrocardiogram, but then a negative reading can occur even in the face of a severe coronary thrombosis. To play safe, the patient was kept in bed for the usual six weeks. After his discharge he had another attack, and this time he was examined by an alert physician who suspected hyperinsulinism. The Glucose Tolerance Test confirmed the diagnosis. The patient responded to treatment and has had no recurrence in four years.

Another case involved a man who had a luncheon appointment with a business prospect. An important sale was to be consummated over the table. When the man found that his guest had not arrived at the restaurant, he decided to wait for him outside in his car. It was a very hot day. The guest was delayed for two hours. Suddenly the waiting man blacked out. An ambulance was called and he was taken to the hospital. Physical examination and the electrocardiograph ruled out the suspected coronary thrombosis. The case was first labeled "heat prostration" in spite of the fact that the victim did not have the high temperature that usually goes with heat stroke. The Glucose Tolerance Test, however, revealed the true state of affairs. The man was treated for hyperinsulinism and recovered completely.

One hesitates to rob Dr. Harris of any credit that is his due, but actually he was in a strategic position to discover hyperinsulinism. As he pointed out, overindulgence in caffeine is a common cause for the condition. Harris conducted his research in Birmingham, Alabama, the heart of the South, where various beverages consisting of sweetened and flavored water spiked with caffeine are water substitutes. Hyperinsulinism may be induced in persons predisposed to the condition by the very combination of caffeine and sugar found in these beverages.

Overindulgence in sweets tends to sensitize the islands of Langerhans by subjecting them to repeated stimulation and exercise. Caffeine stimulates the adrenal cortex to produce more of its hormones, which in turn induce the liver to break down glycogen into glucose which flows into the blood stream. This is why a cup of coffee "gives you a lift." Trouble develops because the islands of Langerhans cannot distinguish between the effects of drinking coffee and eating food. They don't know and don't care whether the sugar has come from the food that is being digested or from previously stored glycogen broken down by the action of the caffeine's stimulus

DIET FOR HYPERINSULINISM

On Arising—Medium orange, half grapefruit, or 4 ounces of juice

Breakfast—Fruit or 4 ounces of juice, 1 egg with or without two slices of ham or bacon, ONLY ONE slice of any bread or toast with plenty of butter, beverage

2 Hours After Breakfast—4 ounces of juice

Lunch—Meat fish cheese, or eggs, salad (large serving of lettuce, tomato, or Waldorf Salad with mayonnaise or French dressing), vegetables if desired ONLY ONE slice of any bread or toast with plenty of butter; dessert, beverage

3 Hours After Lunch—8 ounces of milk

1 Hour Before Dinner—4 ounces of juice

Dinner—*Soup if desired* (*not* thickened with flour), vegetables liberal portion of meat fish, or poultry, ONLY ONE slice of bread if de[illegible], beverage

2–3 Hours After Dinner—8 [illegible]

Every [illegible] 4 [illegible] k or a

Al[illegible]
Brussels [illegible] ca[illegible]
cucumbe[illegible]
sa[illegible]

Allowable Fruits—Apples, apricots, berries, grapefruit, melons, oranges, peaches, pears, pineapple, tangerines

May be cooked or raw, with or without cream but without sugar Canned fruits should be packed in water, not syrup

Lettuce, mushrooms, and nuts may be taken as freely as desired

Juice—Any unsweetened fruit or vegetable juice, except grape juice or prune juice

Beverages—Weak tea (tea ball, not brewed), decaffeinated coffee, coffee substitutes May be sweetened with saccharin

Desserts—Fruit, unsweetened gelatin, junket (made from tablets, not mix)

Alcoholic and Soft Drinks—Club soda, *dry* ginger ale, whiskies, and other DISTILLED liquors

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AVOID ABSOLUTELY—Sugar, candy, and other sweets, such as cake pie, pastries, sweet custards, puddings, and ice cream

Caffeine—ordinary coffee, strong brewed tea, beverages containing caffeine (Your doctor will tell you what these are)

Potatoes, rice grapes, raisins, plums, figs, dates, and bananas

Spaghetti, macaroni, and noodles

Wines, cordials, cocktails, and beer

The first feeding on arising starts the body's machinery, and breakfast builds it up to speed The midmorning juice helps maintain that speed until lunch, while the afternoon milk prevents the late afternoon slowdown, so common in

In the centuries after Botallo, many others described hay fever with increasing detail, notably Bostock in 1819 The first to ascribe the cause to plant pollens was Elliotson a few years later Since then we have accumulated a vast amount of data concerning hay fever and the other allergies but we still do not know why certain persons should be hypersensitive to substances which are completely harmless to others

The official name of hay fever is Seasonal Allergic Rhinitis Chronologically, there are three kinds the early spring the late spring and early summer, and the late summer and early fall The first is caused by hypersensitivity to the pollen of trees, the next to the pollen of grasses, and the third to the pollen of weeds The dates of these periods vary with latitude, altitude, proximity to water, and prevailing winds, and whether the season itself is early, "normal," or late Theoretically, one could escape hay fever by starting to move toward the Arctic Circle in spring, keeping ahead of the allergy as it proceeds farther north The average number of hay fever days per season varies greatly in different parts of the country, from a felicitous zero in Arizona, California, Florida, Oregon, Washington, Nevada, and extreme northwestern Texas, to a baneful 42 days in Dallas, Texas 41 in Hatteras, North Carolina, 39 in Springfield, Illinois, 38 in Peoria and Kansas City, 37 in Indianapolis and Oklahoma City, and 36 in St Louis and Omaha In general it is high throughout the central portions of the country from Texas to Minnesota—33 in Minneapolis, for example, and over a month in most of Tennessee, Kentucky, Ohio, Indiana, and western Pennsylvania and New York It is 35 in Buffalo in contrast with 20 in New York City, 15 at Coney Island, and only 3 a Lake Saranac It declines rapidly with altitude It is fa lower at the top of the Empire State Building than in th street below It is light in most of the Rocky Mountain regio and very low in northern Maine and Michigan

Some unfortunates suffer from all three types of hay fever

They start sneezing when the trees bloom in early spring and don t stop until snow flies in the fall Many persons have two kinds of hay fever, but most only one

For many years hay fever sufferers received little sympathy and much ridicule from nonsufferers who simply could not understand why that which did not bother them should trouble someone else At first there were absolutely no remedies available Except for escape, nothing could be done but to grin and bear it Those who could afford it ran away to areas where there was little or no hay fever Some took a long ocean voyage Pollen does not exist in significant quantities in the air over the sea more than a hundred miles or so from shore, becoming too widely diffused to affect the allergic In the summer and autumn of 1937 the late Dr E E Free a prominent scientific consultant who was a lifelong hay fever sufferer, solved his problem in a novel way He engaged a suite on one of the New York-to-Bermuda ocean liners and spent the hay fever season shuttling between the two places He took along his secretary, files, and equipment and worked on board ship and in Bermuda (where there is no hay fever), holding consultations with clients while the ship was docked in New York The publicity he received stimulated enough additional business to defray the expense

The earliest hay fever remedies were mere palliatives and completely ineffective There were such items for example, as mentholated cigarettes and menthol inhalers There was even a device which one inserted in the nostrils, supposedly to filter out the offending pollen Most victims could not endure the discomfort aside from which the contrivance was not always successful since many pollens were too small to be filtered out

Seasonal Rhinitis unfortunately, is not the only type of hay fever There are other allergic disorders having similar unpleasant symptoms which are caused by an almost infinite variety of substances Some of the most common are fungus

spores, the dander of horses, dogs, cats, and other animals, feathers, wheat, and other flours, industrial dusts, *house dust*, orris root (used in the manufacture of face powder), flaxseed and karaya gum (used in some wave set preparations), kapok, the silklike covering of the seeds of a West and East Indian tree related to the cotton plant, which is widely used to stuff cushions and pillows, and insect scales But this formidable list does not exhaust the substances to which people are sometimes allergic

Those substances are all inhalants, things we inhale with the air we breathe There are other allergens which are ingestants, things we absorb from the alimentary tract when we eat and drink Frank A Simon, a leading authority on allergy, says that "practically any food may act as an allergen' [3] He lists milk, eggs, wheat, tomatoes, spinach, peas fish, and peanuts Many drugs are also allergens, as well as some flavoring and preservative materials, and even tooth pastes and mouth washes'

There are still other allergens which we absorb through our skins The most common is poison ivy There are also poison oak sumac, primrose, and many others that are fairly common Many drugs, chemicals, and dyes are allergens It is probable that the length of the list of allergens is limited only by what so far has been observed and recorded

Both the term, 'allergy," and its concept are relatively new The expression was first used in 1906 by von Pirquet, who felt the need of a new word, not otherwise used that would designate the altered condition which an organism achieves after acquaintance [he used the German word *Bekanntschaft*] with any organic, living, or inanimate poison" For example, an individual who previously has been injected with a serum reacts differently to it than someone who has contact with the given serum for the first time 'He is, nevertheless, as yet far from being immune because of this All that we can say about him is that his capacity to react has been altered I

suggest the word allergy to designate this general concept of altered reactivity" [4] At first the word was used only to designate a *decreased* reactivity, though the idea of *increased reactivity* was not ruled out certainly not by von Pirquet When we use the term today we refer to the *increased* reactivity that is typical of the allergic after he once has been exposed to some foreign substance The capacity of the individual to react is acquired as the result of exposure to the same specific substance

Once this concept was established it was possible to develop a form of treatment called hyposensitization This is the process of making the patient progressively less sensitive to the one or more afflicting allergens by a series of increasingly concentrated subcutaneous injections of those very substances It was first necessary of course to determine which allergens (usually there was more than one) were causing the trouble The patient was given the skin test There were several techniques one of which was to scratch or abrade the skin without drawing blood and then to rub the spots with those allergens that seemed most likely to be the culprits Another was to hold the suspects in close contact with the unabraded skin for several hours by means of adhesive tape Frequently it was necessary to test many allergens before the right ones were found And even then the results were not certain Such an authority as Simon admits that "many positive skin reactions are of no clinical importance Furthermore a negative skin reaction to a certain substance does not prove that the patient is not *clinically sensitive* to that substance" [5]

As we moved forward toward the era of the so-called "miracle drugs one drug after another was hailed as the long sought panacea for the allergy victim only to be later found wanting in one way or another First came the vasostrictors such as *ephedrine* and *benzedrine* During World War II *benadryl* acquired considerable popularity It provided temporary relief, frequently at the cost of dizziness and

chronic drowsiness Another drug which some found more satisfactory was *pyribenzamine* (PBZ) The most recent on the scene were the other antihistamines

All of these remedies provided some degree of relief for some patients None was effective for all In spite of them the best remedy was still an ocean voyage or a trip to some locality not subject to the menace The next best was the complete air conditioning of one s home and office Both of these remedies had the defect in that only the rich could afford them

We speak with the voice of experience, for one of the authors (A W Pezet) has had hay fever since early child hood and has tried everything at least once During the past year the other half of this collaboration (E M Abrahamson) treated him for hyperinsulinism and for the first time in forty six years, except for years spent in California Mexico, South America and other immune places, he was without a single day of hay fever This seeming miracle is no isolated coin cidence as will be seen presently

Even if they have failed to discover the cause, the allergists have learned many interesting facts about the allergies dur ing the past twenty five years They have learned that there is a hereditary predisposition toward allergies as a type of malady Allergies run in families different members of which may develop different allergies more than one each, or none at all Another curious fact which makes the allergies almost unique is that they are pre eminently the diseases of those of relatively higher intelligence *There is a definite correlation* between the hypersensitivity to allergens and intelligence the lower animals, for example, do not have allergies Study of these diseases undoubtedly has been retarded by our in ability to use dogs and cats and rabbits for experimental pur poses

This strange correlation has led the psychoanalysts to the hypothesis that the causes of allergies are purely *mental* Many allergists, in fact, sorely baffled by what one of their

number has called the "strange malady,"[6] "have long suspected that deep seated emotional disturbances lie behind a vast number of the cases that come before them."[7] Recently, Dr. Hyman Miller, associate clinical professor of medicine at the University of Southern California Medical School, and his wife and research partner, Dr. Dorothy Baruch, a well-known Beverly Hills psychotherapist, have reported on a joint research they are conducting. They have attempted to make a "scientific measurement of the relationship between specific emotional disturbances and allergies." At this incomplete stage of their work the Millers "have found that the vast majority of the allergic children who were brought before them had a deeply troubled relationship with their parents—with their mothers especially." In most of the cases there was "maternal rejection"—that is, a mother "whose behavior toward the child is such that she *consciously or unconsciously* has a desire to be free of the child and considers it a burden."

At this point we were reminded of the delightful Myerson anecdote. At a meeting he attended, some psychiatrist advanced the hypothesis that epileptics are men who hate their fathers. Myerson commented that he knew a lot of epileptic cats who had never met their fathers.[8] In this age of the split atom and the flying saucer, however, it is inadvisable to scoff at anything. The Millers do not claim that all allergic children are rejected by their mothers, nor that all rejected children develop allergies. They do claim, however, that 98.4 per cent of the allergic children tested were also rejected children. "Maternal rejection," say the Millers, "is not only an almost universal experience in the lives of allergic children, but they differ in this respect from other groups of problem children."[9] While the assumptions of the Millers may not be correct, the data on which they are based have a most important bearing on the causation of the allergies, as we shall discuss in greater detail later.

Needless to say, the allergists as a body have ignored the

claims of maternal rejection as a causative factor in allergies The medical profession, like other segments of humanity, is composed of a minority who believe in anything that is new and a majority who refuse to believe in anything that is new Between them, the open minded man of science, willing to pick up crumbs from the right and the left but unwilling to put them in his mouth until he has thoroughly tested them has a difficult time of it

During the past quarter century many allergists have interested themselves in blood sugar Several investigators subjected many asthmatics to the standard diabetic two hour Glucose Tolerance Test They found a tendency to low fasting blood sugar levels and, when the patient drank the glucose solution for the test, the rise in blood sugar was less than in normal persons As far as diabetes is concerned, asthmatics are even more normal' than healthy people[10] These observations have been known for many years, but no explanation was offered

A word about asthma It is an allergy identical to hay fever in almost every respect except one It is caused by the same pollens, spores, danders, and dusts, and like hay fever it may be seasonal or perennial It is affected by location and climate and heredity is a causative factor It is probably as common and as widely distributed as hay fever It differs from hay fever

the respiratory tract and the conjunctivae (the pink membranes surrounding the eye) Asthma was first described in the second century by Aretaeus the Cappadocian, the same sage who gave us our first detailed description of diabetes Though known for all these centuries, asthma has remained one of the mysterious diseases that is little understood and for which no effective cure has been devised

If low blood sugar is characteristic of asthma, we should expect asthma to be nonexistent in diabetics whose blood

sugar is high Geneticists found that the two conditions often shared a common heredity but apparently were mutually exclusive They very often occurred in members of the same family but only extremely rarely in the same individual It was thought that some defect occurred in the same hereditary factor which could take either of two directions, giving rise to diabetes on asthma [11]

If there is no relation between the diseases, we should expect that the percentage of diabetics with asthma should be about the same as the percentage of nondiabetics with asthma. Many observers have noticed the contrary, that either disease seems to protect its victim from the other [12] Joslin, the great authority on diabetes, had a few patients who had suffered from asthma but lost it when they acquired diabetes

Asthma frequently is associated with underactivity of the thyroid gland and many asthmatics have been helped by taking thyroid extract [13] One patient a woman, had very severe asthmatic attacks After a number of years of great discomfort she noticed that the attacks became progressively less severe and less frequent, finally ceasing altogether Soon thereafter she lost a great deal of weight She became extremely nervous and developed an unbearable palpitation of the heart These are symptoms of toxic goiter A basal metabolic rate determination confirmed her physician's diagnosis The enlarged and overactive thyroid gland had to be removed After the operation her symptoms disappeared, but the asthma, which had not troubled her for several years, returned

A severe case of asthma, then was arrested by a toxic goiter, an ailment which has long been known to make diabetes much more severe

A few years ago a relationship was discovered between asthma and the amount of potassium in the blood Asthmatics tend to have the element in excessive amounts [14] (A treatment was devised based on this finding, but it did not prove

practicable) By contrast the serum potassium of diabetics tends to be low

The same investigator noticed that asthmatics suffered much more when they ate excessive amounts of table salt On the other hand, it was found that diabetics could get along with less insulin if they were given large amounts of table salt The salt, however, had to be taken by a tube that passed through the mouth and stomach into the intestine because such a large amount of salt was irritating to the stomach This was not proposed as a treatment for diabetes Obviously the needle is far less annoying than the stomach tube But the experiment was performed on volunteers to increase our understanding of the mechanism of diabetes [15]

All of these considerations point to a reciprocal relationship between asthma and diabetes To tabulate

	DIABETES	ASTHMA
Blood sugar	*High*	*Low*
Blood potassium	*Low*	*High*
Effect of goiter	*Makes worse*	*Makes better*
Effect of salt	*Makes better*	*Makes worse*

It seemed fairly well established that asthma and diabetes were opposites Diabetes is hypoinsulinism and the physiological opposite of that is hyperinsulinism Purely as a working hypothesis therefore, it seemed logical to assume that asthmatics actually have hyperinsulinism Naturally that condition would be in a mild form or asthmatics would have the typical symptoms of hyperinsulinism—hunger, fatigue, and so forth If this assumption were correct, the patients tested should not indicate it merely statistically It would not suffice for a majority—even a very large majority—of asthmatics to have hyperinsulinism All asthmatics must have it A single negative finding would be sufficient to demolish the reasoning

Twelve consecutive, unselected patients were treated with

Seale Harris' six-hour Glucose Tolerance Test[16] All of them produced curves which showed a late drop in blood sugar and met all of Dr Harris' criteria for hyperinsulinism (Subsequently these results have been repeated in several hundred cases)

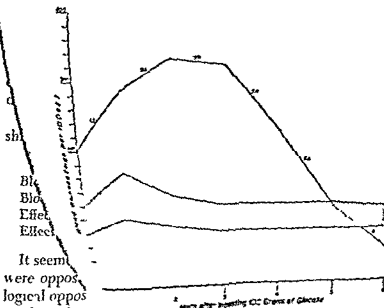
We therefore can say that asthmatics have hyperinsulinism But of course, not all cases of hyperinsulinism have asthmatic symptoms In the language of the mathematician, we can say that hyperinsulinism is a necessary but not sufficient condition for the appearance of asthma[17]

These twelve tested patients were then placed on Harris' diet All of them improved considerably Only two had attacks of asthma after being placed on the diet The twelve were not so fortunate with other symptoms of allergy, such as sneezing and running of the eyes and nose The gratifying response of these twelve patients to the dietary treatment is further evidence that hyperinsulinism has something to do with asthma We cannot say that it is the cause of asthma We *can* say that given the allergic sensitivity, hyperinsulinism apparently permits, if not induces, the spasm of the bronchi that produces the asthmatic attack This is borne out by several other facts

It has long been known that asthmatics have reason to dread the night, for "the beginning [of an attack] is said to be most frequent during the night, when the patient has had his first sleep, for instance, at two or three in the morning he suddenly wakes with a stuffy feeling in his chest, and within a short time he is in the throes of an attack of asthma"[18] If pollen were the only factor, asthmatic attacks should be more common in the daytime when flowers are open and discharging their pollen into the air Yet, these nocturnal attacks are not fortuitous The blood sugar in persons with hyperinsulinism reaches its minimal value at precisely those hours During the day meals are usually frequent enough to prevent a decided fall in blood sugar in persons with *mild* hyperinsulinism

whenever her breathing became too labored, she would step into a telephone booth to give herself an injection of adrenalin.

On November 12, 1939 she was given the six hour Glucose Tolerance Test. The results were so startling that we include the graph of her test here.



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tively low for her, only 200 The normal fasting blood sugar range, of course, is between 80 and 120 Her wheeze disap-

of blood at hourly intervals and analyzing them for sugar. When the drop occurred, the wheeze returned Finally her blood sugar level dropped below the normal range and the test had to be stopped by giving her some food

If the test had been conducted for only two hours, it would have revealed diabetes Such a case of simultaneous diabetes and asthma would have destroyed our hypothesis There had been an abnormally large rise, however, and the level did not reach the initial value in two hours These are indications of diabetes By prolonging the period of investigation, it was seen that the rise was followed by a dip into the abnormally

tion to some delay in the production of insulin so that once released it is secreted too liberally This enables the patient to

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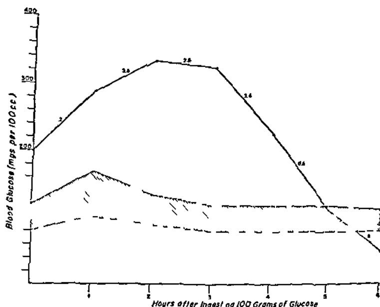
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have a complete explanation of why it is possible for the patient to have both diabetes and asthma Her treatment previous to this discovery had, of course, been a little ridiculous She had been taking insulin for her diabetes, thus lowering her blood sugar and making her asthma worse When she then took adrenalin for her asthma, she raised her blood sugar level and made her diabetes worse The repeated injections of the two drugs made both conditions worse and necessitated steadily increased doses of both drugs A vicious cycle with a vengeance!

The discovery led to a rational treatment for her antago-

whenever her breathing became too labored, she would step into a telephone booth to give herself an injection of adrenalin

On November 12, 1939 she was given the six hour Glucose Tolerance Test The results were so startling that we include the graph of her test here



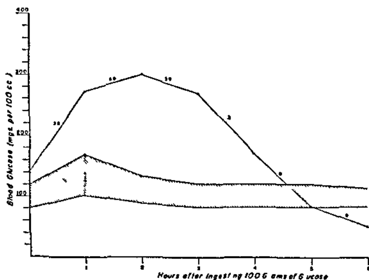
7—*Asthma and Diabetes* (1)

This curve accounts for the simultaneous occurrence of diabetes (hypoinsulinism) and asthma (*which we believe to be accompanied by* hyperinsulinism)

She had promised not to take any adrenalin during the night before her test It will be remembered that adrenalin causes the liver to discharge some of its glycogen into the blood in the form of soluble glucose But she had found it urgently necessary to take an injection of adrenalin in order to be able to breathe She was wheezing slightly when she came in for the test Her fasting blood sugar was compara

care She replied that she had required six or seven injections daily The allergist still was not convinced even after she had told him that since being treated for her dysinsulinism she had not needed adrenalin for six months! Such is the tyranny of routinized thinking even in an outstanding specialist Is it any wonder that the rank and file of the medical profession are slow to adopt a revolutionary change?

Another patient with both asthma and diabetes had an almost identical experience Although this patient drank coffee



8—*Asthma and Diabetes* (2)

on occasion she was sufficiently faithful to her diet not to require any adrenalin She received a postcard from the allergy clinic asking why she had neglected treatment for so many months Her chart had the interesting notation written in the allergy clinic "Sleeps on a feather pillow, contrary to advice!" (The exclamation point was on the original notation from

nistic conditions She was taken off both drugs and given the Harris diet Of course, the interdiction of adrenalin was not sudden—she could not sweat out her cure, she had to breathe But she soon found that she could get along with progressively less adrenalin She finally was able to abandon its use entirely Her diabetes was very mild and she passed under 10 grams of sugar daily meeting our criterion for good control In effect, we permitted the asthma and diabetes to neutralize each other

For a while the patient followed her dietary instructions religiously, but then she slipped and drank coffee After a few weeks the wheeze returned She had the good sense to give up coffee for good, and the wheeze disappeared again, never to return

This patient was brought before a medical group A famous allergist was in the audience In his discussion he claimed that the treatment was not scientific because "it was assumed that the patient had hyperinsulinism" It was impossible to convince him that the assumption was a working hypothesis that was completely justified by the results He talked of allergens, the various substances capable of inducing allergies He also spoke of atopens, which are nothing more than a more limited type of allergen ("By atopy," wrote Coca, who introduced the term, "is meant certain clinical forms of human hypersensitivity that do not occur, so far as is known in the lower animals, and which are subject to hereditary influence In this category have been included thus far only asthma and hay fever, but it is generally thought that eczema and certain forms of drug and food idiosyncrasy will eventually be placed with these" In other words an atopen is an allergen restricted to the commonest forms of allergy! Unfortunately, medical science is full of such words which have their specific uses but which are too often used as a smoke screen

The patient had been treated in this allergist's clinic. She was asked how much adrenalin she took while under his

while the damage done by rheumatic fever is not so obvious to the naked eye

Although rheumatic fever very frequently follows an upper *respiratory infection such as an attack of tonsilitis* no infective agent has been proved to be its cause There is apparently some hereditary predisposition to rheumatic fever for it is rather common in some families A certain physical type seems more susceptible to it than others—the fair haired blue eyed light skinned type with a tendency to freckle Environment plays an important part too for it is most frequent in cold damp climates and during the cold damp months It has been called "acute" rheumatic fever but that is a misnomer for the cases never really come to an end Patients are subject to periodic "exacerbations —repeated out breaks—when the smoldering fire bursts into flame

There is a great deal of evidence to support the view that rheumatic fever is an allergic reaction to a focus of infection in the tonsils Some of the skin manifestations (*erythema multiforme* and *erythema nodosa*) resemble hives (*urticaria*) and the rashes produced by allergy to inoculations [28] Since hyperinsulinism is an attendant condition in other forms of allergy the question naturally arises is it also in rheumatic fever? In answer to this there is the supporting evidence that diabetics seldom show signs of rheumatic heart disease [29] Against this is the understanding that diabetes is usually a disease of late adult life whereas rheumatic fever rarely occurs after childhood But the latter statement is true only of the initial attack of rheumatic fever Not all children succumb and most of them reach adult life Consequently unless there is some antagonism between the two diseases there is no reason why adults who had rheumatic fever in childhood should not acquire diabetes in about the same ratio as the general population

Several patients who had recently recovered from attacks of rheumatic fever were subjected to the same hyperinsulin

which this was quoted) The same chart contained a notation written in the diabetes clinic It read "BUT SHE HAS NO ASTHMATIC ATTACKS!!!"

Several other patients were investigated in the same fashion They all followed the same pattern[26]

This success led to the investigation of that other common allergic condition—hay fever Hay fever patients tested exhibited the same type of hyperinsulinism sugar tolerance curve They were helped considerably by the diet, but they still experienced morning sneezes (when the blood sugar is low) Their eye symptoms were not relieved much[27] This was a puzzle for many years Now, however, we can arrest hay fever too This will be discussed in a later chapter

Rheumatic fever which has been known since the sixteenth century, is one of the most devastating diseases of childhood It has been estimated that more than 10 per cent of the deaths occurring before the age of eight are due to acute rheumatic fever and its sequelae (the diseased condition that follows a disease) There must be close to two hundred thousand cases a year in the United States, and at least one million Americans now bear the marks of rheumatic infections suffered in childhood Rheumatic fever is not a reportable disease,' so that these figures are only estimates but they are conservative estimates Everyone who has suffered from rheu [illegible] some damage to his heart This may be [illegible] very severe [illegible] per cent of all cardiac deaths (which lead all others and now number close to four hundred fifty thousand a year) are due to rheumatic fever Compared with this dread killer and maimer, poliomyelitis fades into insignificance Why, one might ask is so much more public attention accorded to infantile paralysis than to rheumatic fever? We believe it is because of the visual impressionability of the public Polio cripples visibly,—

The diet of the poor is usually heavy in such foods as bread spaghetti and especially potatoes—all carbohydrates—because they are relatively cheap The preponderant incidence of rheumatic fever in the slums is well known A team of English investigators noticed and commented upon this dietary imbalance among rheumatics They gave the children under their care more liberal quantities of milk and cream There was no significant reduction in the number of their attacks of sore throat but the rheumatic attacks dropped to one third of what they had been [32]

Unfortunately neither of these groups of investigators used the Glucose Tolerance Test Nevertheless it would appear reasonably well established that the changes in diet were related to lessening their patients susceptibility to rheumatic fever attacks Both groups used measures that tend to diminish insulin secretion Their success was only partial because they did not complete treatment with the Harris regimen

This conception of the hyperinsulinism factor in rheumatic fever was also confirmed by animal experimentation It had never been possible to produce the lesions of rheumatic fever in animals Foci of infection with those organisms that had been suspect of producing rheumatic fever in humans had created only local abscesses generalized blood stream infections and so forth Th not produce rheumatic lesions
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ism investigations that had proved fruitful with other types of allergies The results completely vindicated our theory [30] Patients treated with the Harris diet went through two winters without a single exacerbation, although most of them had a sore throat or two during each cold season

This experiment was followed by the examination of a group of "inactive" cases—persons who had not had any *recent* attacks It was found that these people could be divided into two groups The first group had had several exacerbations The Glucose Tolerance Test showed that all the persons in this group had hyperinsulinism After following the diet for a while, they were able to report that they had had no more attacks of rheumatic fever in spite of episodes of sore throat The second group of persons had had only one attack of rheumatic fever and that many years before The persons in this group did not show a drop in blood sugar following the ingestion of the glucose solution They did not have hyper insulinism Their dietary history was gone into in detail It was learned that these people never drank coffee and that they didn t care for sweets In other words, their long habit of doing without the exciting causes of hyperinsulinism had removed that factor which is apparently necessary for the development of allergy to the infection in their throats

It is interesting that this work was confirmed before it was performed Coburn and Moore, who had been working on the problem of rheumatic fever for many years, reported that all of the patients they investigated had been eating too little protein All other factors including minerals and vitamins were entirely adequate They put their patients on a diet with more protein food Simultaneously, of course, they had to cut down on the carbohydrates to prevent fattening them After going on this diet none of them had any rheumatic attacks although they continued to have sore throats In effect, they had given their patients much of the Conn diet, which also eliminates hyperinsulinism [31]

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Of course not all cases of rheumatic fever occur in the slums Why do the children of more affluent parents get the disease? It is easily demonstrated that well to-do rheumatic children are finicky eaters They eat large amounts of sweets, which their more fortunately situated parents can afford The parents usually are so happy to have these children eat

anything at all that they gladly indulge their dietary whims

The theory seems to be justified that there are several factors necessary to the development of rheumatic fever First there must be a focus of infection Second there must be an inherent allergic susceptibility which third by improper diet is fully developed The combination of all three factors is necessary to produce rheumatic fever The final piece of evidence offered in support of this view is the fact that rheumatic persons are susceptible to and often acquire one or more of the other allergies The evidence is in the record of innumerable case histories

Another disease which like asthma hay fever and rheumatic fever only rarely occurs simultaneously with diabetes is peptic ulcer This is fortunate indeed because it would be difficult to devise a diet to care for both conditions In ulcer we feed the patient large amounts of fat a food which we avoid in the modern treatment of diabetes [34] On the other hand a high intake of carbohydrate is of benefit in diabetes because it tends to keep the blood sugar level lower Such starches are avoided in cases of ulcer

There are many statistical studies that confirm the widely held opinion that the two conditions only rarely occur together [35] Joslin believes that this can be explained by the difference in the ages at which people usually have the two conditions [36] Ulcer is a disease of early adult life diabetes of later occurrence. We do not believe that this satisfactorily explains the fact In the first place once acquired in early adult life ulcers tend to become chronic While they are not cured one does not die of them One learns to live with them This is corroborated by the low death rate from ulcers—only 5 8 per 100 000—against 24 8 for diabetics in spite of all that can be done for them Consequently we should expect the majority of ulcer patients to survive to the diabetic age Furthermore unless there is some other factor working to pre

vent it, the high fat diet given to ulcer patients should predispose them to the later acquisition of diabetes[37] Yet no evidence has ever been submitted to indicate any particularly high incidence of diabetes among treated ulcer patients

It has been generally recognized by the medical profession that ulcers and gall bladder disease tend to occur in two distinct constitutional types which differ sharply in many respects[38] This gall bladder type is very frequently diabetic Unless all our ideas about constitution and disease are wrong we should expect the opposite type to be relatively free from diabetes That the restriction of fats helps to keep gall bladder patients freer of symptoms also suggests that gall bladder disease and diabetes attack similar constitutional types

But no matter what the true explanation may be experience in most diabetes clinics will show that very few of their patients have peptic ulcer (This discussion demonstrates the difficulty in drawing valid conclusions from statistical analyses The complexity of biological phenomena leads us to make simplifying assumptions in order to reduce the number of variables We can thus bring the problem within the limited powers of human reasoning But we are actually bending the solution to our mind s desire Too often we have begged the question)

rapid and frequent constrictions of the stomach after meals that is characteristic of peptic ulcer[40] There is indeed good reason to believe that these spasms which simulate those of organic lesions in the stomach and duodenum may actually be the precursors of the development of ulcers

The assumption that peptic ulcer, like asthma, hay fever and rheumatic fever is associated with hyperinsulinism was subjected to direct experimental verification To avoid the pitfalls of reasoning from statistics, it was made a condition

*dys*insulinism The first portion of each is typically diabetic Then they topple into the low blood sugar range in the precipitous manner that proclaims the strange dysinsulinism condition

All of these peptic ulcer patients were treated with the *Harris diet for hyperinsulinism* The patients did quite well on it None of them had to take alkalies for longer than a few weeks while many of them did not require any at all The dysinsulinism patients were treated exactly like the others since their diabetes was mild enough to be ignored It is an interesting coincidence that the modified Sippy diet widely used in the ambulatory treatment of peptic ulcer greatly resembles the Harris hyperinsulinism diet We find that the prohibition of coffee, which is a part not only of the Sippy but of all ulcer regimens, on purely empirical grounds, is now seen to have a rational, scientific basis

It must be mentioned that none of these cases of peptic ulcer, as with the cases of asthma, hay fever, and rheumatic fever that were studied exhibited any of the *major* symptoms of hyperinsulinism such as ravenous hunger, acute fatigue, sweating, or palpitation These symptoms are to be found only in marked cases of the disease But a moderate hyperinsulinism that accompanies other conditions and can be revealed only by the six hour Glucose Tolerance Test would seem, as a result of these investigations to be fairly common

We cannot say positively that hyperinsulinism precedes an ulcer and is causally related to it, but there is *some justification* for believing that such is the case Several cases were investigated which differed from known cases of anatomical peptic ulcer only in the absence of positive X-ray findings According to all the symptoms they were otherwise peptic ulcer cases They had the same typical curves for their Glucose Tolerance Tests They responded to the identical dietary treatment They were in every way ulcer cases except that no visible ulcer could be seen on the X ray plate This is signifi

cant something that future investigations should clear up

So far we have presented *facts* which have been verified by scientific experimentation with unanimous—not merely statistically promising—results Consequently a bit of speculation would not now seem unjustified

It has been shown that hyperinsulinism has been found to be a condition necessary to the development of such diversified diseases as ulcer asthma and rheumatic fever All of these conditions are markedly constitutional diseases The protean nature of hyperinsulinism becomes understandable when we consider the effect of chronic low blood sugar The normal level of blood sugar is *not* the 80 to 120 mg per 100 cc of blood given in the medical books That is the normal *fasting* level and fasting is not a normal condition It produces the unpleasant sensation of hunger which leads to its prompt relief The really *normal* blood sugar level during the waking working and eating hours of the day fluctuates about a mean of 140 mg per 100 cc In hyperinsulinism this level is considerably lower and we have in effect a state of chronic partial blood sugar starvation But sugar in the form of glucose is used to nourish all the cells of the body Their health requires an adequate amount of glucose at all times If inadequate nourishment is long continued we can expect some weak spot to break down sooner or later We cannot predict where the break will occur just as we cannot be certain where the automobile persistently running on too lean a mixture will give trouble

During World War II an X ray specialist was in charge of the X ray department at the post hospital of a large army camp He made rather frequent diagnoses of peptic ulcer which angered his commanding general Unknown to the specialist the general sent a number of the X ray plates to the Mayo Clinic for interpretation The diagnosis of ulcer was confirmed in every case

It was noticed that the incidence of peptic ulcer among

servicemen was much greater than it had been in World War I. Psychosomatic medicine was now in great vogue. It was held that the increase was due to the greater difficulty in adjustment to military life. We do not believe that the difficulty of adjustment in the training camps was any more severe than in World War I. Certainly if such a thing were a cause for ulcers, there was a much greater cause in the combat divisions where men were shooting with live bullets and not merely practicing. But the incidence of ulcer among the combat divisions was much less than in the training camps. In the light of the revelations we have made, there is a simple explanation for this supposed phenomenon. Anyone ever connected in any way with military life has seen the soft drink dispensing machines in every building of all cantonments. The men coming off training maneuvers were hot and thirsty. Frequently there was no really cold water to drink; these machines with their ice cold sweet drinks were quite handy. The men would drink several bottles at a time. Among combat troops, however, the stuff frequently was rationed at three bottles per man per week, if that. This, we believe, is why there were fewer cases of ulcer among the combat troops than in the camps, and fewer in World War I than in World War II. The men were getting less *caffeine*.

Americans are the largest consumers of coffee in the world. Not content with that excessive use of caffeine in the fine aromatic and ancient *caffa* of Abyssinia, we have concocted and popularized by stupendous high pressure advertising a host of soft drinks previously unknown to the civilized world. These sugar laden and caffeine containing carbonated beverages are imbibed by adult, teen ager, and even children in an ever increasing and staggering volume. They are without [illegible] of d seases that

he matter

5

Body, *Mind*, and Sugar

RICHARD H HOFFMANN—NEUROSES AND HYPERINSULINISM—THE MODIFIED GLUCOSE TOLERANCE TEST—THE TAPERING OFF DIET—MORE CASE HISTORIES—SIDNEY A PORTIS—LIFE SITUATIONS—FATIGUE —CIGARETTES— THE TIRED BUSINESSMAN

So FAR we have been concerned with the *body* and with *sugar* as it affects the body Now let us turn to the *mind*

In 1945 Dr Richard Horace Hoffmann asked me (E M Abrahamson) to work with him An eminent psychiatrist Dr Hoffmann had devoted his medical career to the treatment of countless "neurotics" My experience on the other hand had been in metabolic diseases In the course of some twenty years I had seen several thousand diabetics and during the previous ten years I had become acquainted with hyperinsulinism through my research in that field I asked Dr Hoffmann why he wished to form such an unusual association—a psychiatrist and an internist When I heard his answer I quickly accepted the flattering offer

The answer? This story

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ages are imbibed by adult teen age ... ever increasing and staggering volume They are without doubt having some effect upon the incidence of diseases that result from chronic partial blood sugar starvation The matter deserves immediate serious consideration

5

Body, *Mind*, and Sugar

RICHARD H HOFFMANN—NEUROSES AND HYPERINSULINISM—THE MODIFIED GLUCOSE TOLERANCE TEST—THE "TAPERING OFF" DIET—MORE CASE HISTORIES—SIDNEY A PORTIS—LIFE SITUATIONS— FATIGUE'—CIGARETTES— THE TIRED BUSINESSMAN'

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The answer? This story.

mann went to the patient s room He sniffed the air and detected a urinous odor on the patient s breath He asked his colleague if the urea nitrogen of the blood had been determined It had not The patient was on the verge of uremic coma from Bright s disease She had not answered her psychiatrist s questions because she was not completely aware of being questioned

That s something I don t want to happen in my office" Dr Hoffmann told me

Dr Hoffmann is an excellent clinician He believes that most neurotics are the way they are because some underlying and undiscovered bodily ailment contributes to their anxiety Like me he feels that the expression psychosomatic was poorly chosen because so many people read into it a causative relation that was not originally intended The notion that the mind *causes* somatic disease makes the tail wag the dog

After our association had continued a few months we discussed the problem of blood sugar in neuroses Dr Hoffmann had been interested in blood chemistry in psychiatric disorders for many years Curiously he had but one diabetic patient She had been "inherited from his father who was not a psychiatrist and she was not neurotic

A person on whom a diagnosis of diabetes is made experiences a severe emotional shock He realizes that he has an incurable disease—one that can only be arrested and controlled and with which he will have to live by exercising rigorous self denial punctuated with daily stabs of the dreaded insulin syringe One would expect a person experiencing such an emotional shock to become highly disturbed But the experience of practically every diabetes clinic reveals the

astonishing fact that diabetics are, as a rule, very phlegmatic people Indeed, it is usually the doctor who has to worry about their condition for them Diabetics are notoriously uncooperative They seem either unwilling or unable to treat their malady with its merited respect Cajolery, explanation, and even stern warnings and threats seem inadequate to break down the cavalier attitude most diabetics display toward their illness The diabetes specialist is repeatedly struck with the futility of even attempting scientific control of his patients, especially because diabetes is the disease par excellence in which the patient's cooperation is of the utmost importance The death rate of 28 4 per one hundred thousand for a disease from which no one now needs to die—a rate equal to that from fatal motor vehicle accidents—attests to the appalling indifference of most diabetics

Diabetics are singularly unaffected by many ills to which flesh is heir, and we have seen how often hyperinsulinism accompanies those conditions It has been recognized that manifest hyperinsulinism can be accompanied by many psychic phenomena—depressive states, anxiety, and other symptoms that have been lumped together as "neuroses" [1] A masterly review in the *Oxford Looseleaf Medicine* states that "hypoglycemia [low blood sugar] as a disease entity should be kept in mind constantly by all physicians, particularly those doing neuropsychiatric work When seen for the first time and in the absence of a good history, the attack [of low blood sugar] may suggest some brain diseases, such as infection, neoplasm [tumor], or vascular accident [apoplexy] Because of their paroxysmal nature, the attacks may suggest epilepsy, acute alcoholism, amnesia, or some functional disorder such as hysteria It is for these reasons that patients with hypoglycemia frequently are referred to neurological or psychiatric clinics" [2]

A group of two hundred and twenty "neurotic" patients in whom the primary complaint was a mental depression or

when the patient is suspected of having a severer form of the condition If the blood sugar level at 10 A M is below 70 milligrams per 100 cubic centimeters, the diagnosis has been confirmed, and the patient may be fed If it does not fall below 70 milligrams, the blood sugar level is determined again at 11 A M If this examination does not reveal a drop, the test is abandoned The patient does not have hyperinsulinism

Those 'neurotic' patients with hyperinsulinism were all placed on the modified Harris diet After about a month the Glucose Tolerance Test was repeated to see if the somatic condition had subsided It was soon discovered that this was a most undesirable procedure The large dose of unaccustomed sugar 'upset the applecart,' and the patients suffered a recurrence of their original symptoms The absence of tenderness in the left upper quadrant of the abdomen—the presence of which Harris had found to be the only *sign* of hyperinsulinism—is now a sufficient and very satisfactory indication of the return to normal The tail of the pancreas where most of the islands of Langerhans are located becomes sensitive to pressure in hyperinsulinism This sensitivity is a true sign, not a symptom It can be observed objectively by the examiner, because the abdominal muscles go into spastic contraction to protect the sensitive underlying structures When the condition of hyperinsulinism has been corrected the tenderness and spasm are not elicited

It was soon discovered that it was too great a shock to the body to allow the patient to discard his diet all at once To step down gradually toward normal feeding, the diet was modified to the following

After a few weeks on this modified diet the patient was permitted to eat a sweet dessert once a day with the heaviest meal With continued improvement the diet was completely abandoned, except for three final instructions the patient was to dilute his sweets with intelligence, he was to shun caffeine in all forms, and he was *always* to eat a bedtime snack

✓ MODIFIED HYPERINSULINISM DIET FOR TAPERING OFF

Breakfast—Fruit or juice, cereal (dry or cooked) with milk or cream and/or 1 egg with or without two slices of ham or bacon, only one slice of bread or toast with plenty of butter, beverage

Lunch—Meat, fish, cheese or eggs, salad (large serving of lettuce, tomato, or Waldorf salad with mayonnaise or French dressing), buttered vegetables if desired, only one slice of bread or toast with plenty of butter, dessert, beverage

Midafternoon—Glass of milk

Dinner—Soup if desired (not thickened with flour), liberal portion of meat, fish, or poultry, vegetables, potatoes, rice, noodles, spaghetti, and macaroni (may be eaten in moderation *only with this meal*), one slice of bread if desired, dessert or crackers and cheese, beverage

Bedtime—Snack (milk, crackers and cheese, sandwich, fruit, etc)

All vegetables and fruits are permissible Fruit may be ✓ cooked or raw, with or without cream but without sugar Canned fruits should be packed without sugar

Lettuce, mushrooms, and nuts may be taken as freely as desired

Juice—Any unsweetened fruit or vegetable juice except grape juice or prune juice

Beverages—Weak tea (tea ball, not brewed), decaffeinated coffee, coffee substitutes May be sweetened with saccharin.

Desserts—Fruit, unsweetened gelatin, junket (made from tablets, not from mix)

Alcoholic and soft drinks—Club soda, *dry* ginger ale, whiskies, and other DISTILLED liquors

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AVOID ABSOLUTELY—Sugar candy, and other sweets cake, pie, pastries, sweet custards, puddings, and ice cream Caffeine—ordinary coffee, strong brewed tea, and other beverages containing caffeine

Wines, cordials cocktails, and beer

The patients responded amazingly well to this treatment Following are a few typical cases

1 *T K, male, 43 years old* For six years he had upset his family with violent temper tantrums, invariably at mealtime He was generally quite amiable, however, after eating Obviously his attacks occurred when his blood sugar level was low After a few weeks on the diet, the patient reported that the tantrums had abated and finally disappeared

2 *B L, female, 47 years old* For twenty years she had suffered from claustrophobia She refused to enter a vehicle or an elevator, and would never go out unaccompanied After some three weeks on the diet, she found the courage to ride the subway—for the first time in her life! At first she demanded companionship but eventually she traveled alone Within six months she gained twenty much needed pounds and changed from a scrawny, prematurely aged person to an alert, vigorous woman

✓ 3 *S I, female, 21 years old* She was shy, diffident, introverted Despondent over her sick mother, the girl was obsessed with the fantasy that the woman had cancer and would soon die, and that she herself would commit suicide She suffered apprehensive nightmares from which she would awaken in a cold sweat (the result of the extreme drop in blood sugar) She brought reports from the many physicians

who had examined her stating that she had low blood pressure, anemia, and "tissue starvation" A week after starting the diet she began to feel better and soon lost all her fears

4 *J P, male, 38 years old* He was phobic and apprehensive Both his parents had died of cancer and he was obsessed that he too would succumb to that disease He neglected his business to work in the cancer movement but without relief He became gloomy depressed and antisocial and suffered chronic fatigue headaches and vague abdominal distress After being on the diet for two months he returned to his work with renewed interest and ambition (After a period of good behavior he went on a sweet spree but was brought to his senses when his depression recurred) By now he has forgotten his preoccupation with cancer

5 *E W, female 54 years old* This woman had a long history of depression During the preceding 17 years she had been out socially only four times! She had consulted more than sixty doctors and had been in more than twenty sanatoria Her last trip to a sanatorium was at the suggestion of a psychiatrist who prescribed shock treatment, but the resident physician wisely dissuaded her from it In addition to her psychic complaints she suffered from violent menopausal symptoms She was placed on the diet on a Tuesday The following Saturday evening she asked her husband to take her to a motion picture for the first time in years! She has continued to improve and except for her severe menopausal flashes, feels quite well

This case illustrates the grave danger of the improper selection of cases for shock treatment Shock once was considered a panacea for all psychic ills, but we now know that it is advisable only for maniacal conditions Shock renders the depressed person inert so that he no longer burdens his family and friends with his complaints It is fine for those who have contact with the patient—they are relieved of an irritation but the patient himself is still further depressed The effect

shock on a depressed person is an exaggeration of that of sedative and only makes his condition worse

Usually the so called neurotic—the individual who finds difficult to adjust to his environment—is so engrossed wi his misgivings that he is difficult to question and impres Like light struck photographic plates, his brain cells take di and foggy pictures of suggestions made to him He is "neg tivistic —so self interpretive as to be impervious to whatev reaches his mind from without He listens more to his inn voice forming the next question *he* is going to ask or to th next complaint *he* is going to make, than to the most sincer adjurations of the psychiatrist His brain is ill nourished an tired from attempting to work without adequate fuel Hi fatigue has begotten apprehension and his apprehension ha sired distortion Frequently he complains of many somati ills

Earlier it was pointed out that while chronic partial suga starvation of the body s cells eventually would affect som 'weak spot, the location of such a spot could not be pre dicted Now, however we can qualify that statement Sinc the cells of the brain are those that depend wholly upon th moment to moment blood sugar level for nourishment the are perhaps the most susceptible to damage The disturbingl large and ever increasing number of neurotics in our popula tion makes this clearly evident

After restoration of the proper nutrition to the brain these so called neurotics rapidly became more receptive to psy chiatric persuasion It was then that they could begin to see where the shoe pinched where the square peg had been jammed into the round hole where, in short, they had come into conflict with many aspects of life And soon such patients ceased to be neurotic and were able to return to contentment in profitable pursuits We may say that these patients had suffered from hunger not only of the body but also of the mind

When their brains were bathed in a nutrient fluid richer in sugar, they were again able to take "fortune's buffets and rewards with equal thanks"[4]

In support of these findings, Fabrykant and Pacella have reported electroencephalographic (brain wave) changes in hyperinsulinism[5] It has also been shown that mental patients lack the ability to mobilize sugar in response to mental stress[6] It is felt that this failure to respond normally is due to the fact that an excess of insulin smothers the action of the adrenal hormones to which it is antagonistic

Of the two hundred and twenty patients who were first subjected to the Glucose Tolerance Test, two hundred and five were shown to have hyperinsulinism All were successfully treated by means of the modified Harris diet (and by injections which will be described later) The treatment has been continued with almost seven hundred patients at this writing In EVERY case in which the Glucose Tolerance Test has shown that hyperinsulinism was present—and these were more than 90 per cent of the total number—the patient lost his purely psychic symptoms within ten days of initiating the treatment But another month or more is required to make the treatment stick Several patients have learned by bitter experience that they must never take caffeine in any form In fact, caffeine is so much of a causative factor in this kind of depression that the condition might be regarded as a form of caffeine poisoning The reputed and widely accepted harmlessness of caffeine must be thoroughly reinvestigated in the light of this new knowledge

[illegible]

these were not intended to be symptoms of hyperinsulinism When this list was compiled, not only hyperinsulinism but

insulinism that he has made a unique and important contribution

It is a popular belief that long-continued worry and anxiety may bring on such diseases as cancer and peptic ulcer There is no direct scientific evidence of this There is however, considerable psychiatric and even medical literature on the effect of emotional impulses on the somatic system "It is well known," says Dr Portis, "that continued physiologic activity in a tissue may lead to either hypertrophy or hyperplasia, depending upon the type of tissue" Hypertrophy is an increase in the size of a tissue or organ that occurs independently of the growth of the body Hyperplasia is an excessive development of a tissue due to an increase in the number of its cells

As far back as 1927, J La Barre and his associates had performed a series of experiments on dogs which revealed the role of the central nervous system in the control of pancreatic secretions From these studies made in France we know that the pancreas, which is an end organ, is subject to stimulation through the *vagus* the pneumogastric nerve which originates in the medulla oblongata and is distributed by many branches to the ear, pharynx, larynx, heart, lungs, esophagus and stomach Portis made the bold assumption that the low blood sugar of his psychoneurotic patients was due to a long continued stimulation of the right vagus nerve "The assumption was based upon the hypothesis that emotional processes occur somewhere in the highly integrated cortical and that the emotional impulses first go through the hypothalamus [a group of ganglia—the nervous system's switchboard—on the ventral side of the brain] and are relayed to the sympathetic and parasympathetic portions of the automatic nervous system this stimulation might lead to increased activity and irritability of the cells of the islands of Langerhans" This "might be temporary or prolonged, depending on the degree and duration of the . . emotional impulses"

To test the validity of his assumptions Dr Portis studied a large group of patients whose outstanding symptom was fatigue which could not be explained by thorough physical and routine laboratory investigation including a determination of their fasting blood sugar levels This varied in the one hundred and fifty seven patients from normal through somewhat subnormal to definitely low values Largely because their attacks of fatigue came on at regular intervals related to their mealtimes he made further blood sugar level tests His experience and conclusion that a single determination of blood sugar is meaningless are in complete agreement with ours

At this point it should be pointed out that Dr Portis did not employ the six hour Glucose Tolerance Test with which you are now familiar In that test the glucose is administered orally Dr Portis felt that oral administration might *prejudice* the results Gastrointestinal motility is readily influenced by emotional factors and the rate of absorption of dextrose [glucose] from the gastrointestinal tract is affected by motility and by cellular changes in the wall of the intestine Instead he used a three hour test in which the glucose (only 50 grams) was administered intravenously (See Figure 9 p 123) He felt this had a further advantage over the oral test in that "the initial increase of blood sugar is far greater with the intravenous than with the oral test, so that one can logically expect a greater immediate response in secretion of insulin" We on the other hand prefer the oral test because it avoids the necessity of preparing a sterile solution and it spares the patient a puncture of his vein Furthermore, the liver normally gets its glucose through the portal vein and in this test it reaches its destination through the hepatic artery Since the insulin gets to the liver through the portal vein in the oral test, we feel that it more closely approximates physiological conditions It is not too important however, which test is used,

effect on the internal vegetative processes It is well known that perfunctory activity performed without emotional participation is more fatiguing than even strenuous activity performed with emotional participation Clinical observations seem to indicate that fatigue and apathy developing during activity performed without interest are not merely subjective emotional states but are based on the lack of adaptation of the carbohydrate metabolism to the effort required from the organism"

In other words, to do work adequately, whether it be mental manual or a combination of the two, requires a blood sugar level high enough to supply the normal demands of muscle, nerve, and brain cells Without that proper level of blood sugar, work is not performed economically A strain is placed upon the functioning of the body and brain which *becomes progressively injurious to them* *The brain, especially*, needs sugar at all times What maintains the blood sugar at a proper level is apparently a proper balance between the sugar repressive functions of insulin secreted in the islands of Langerhans of the pancreas and the sugar releasing functions of the hormones from the adrenal cortex

In normal routine operations of work and of play it is the emotions of interest, zest, and enthusiasm that stimulate the ... organs as it

and work is nevertheless performed, fatigue results and the resulting fatigue gives further excuse for regressive wishes and thus a vicious circle is initiated" It is the vicious circle of hyperinsulinism, a condition of chronic partial sugar starvation which must become progressively worse unless that vicious circle is broken by placing the victim on the proper diet

The proper diet is a matter about which Dr Portis and the medical member of this team of authors do not see eye to eye

in every detail There is absolute agreement, however, on [illegible] differ somewhat as to how this dietary result is to be obtained Dr Portis utterly forbids alcohol and tobacco but is more lenient in regard to some of the common starchy foods He also permits coffee He overcomes the effects of the starches and caffeine by administering atropine or some other belladonna preparation, which depresses the activity of the islands of Langerhans through the involuntary nervous system Dr Abrahamson, on the other hand, feels that the rigid diet enables the patient to accomplish his aim—quieting the oversensitive insulin apparatus—without the use of drugs We cannot and should not take medicine indefinitely, and it is better, he feels, not to use any drugs routinely, since they require another adjustment when they are abandoned As far as smoking is concerned, he is in complete agreement with Dr Portis in forbidding any smoking before meals As a matter of fact, one cigarette before breakfast does more harm to anybody than twenty afterward He feels that the harm done to frayed nerves by withholding the soothing pleasure of smoking can be greater than that produced by an occasional smoke

Smoking, of course, is not *good* for anyone In considering its harm one must make a distinction between the average "pack-a day" smoker and the "chain" smoker—the moderate smoker and the individual who smokes almost throughout his waking hours, consuming two or more packages of cigarettes a day American businessmen (about whom we shall have much to say) as a class are among the chain smokers According to one authority,[13] 62 per cent of them smoke more than the average pack a day, 27 per cent smoke two, and 21 per cent more than two packages a day! Such excessive smoking permits a great deal more tars and acids, as well as nicotine, to be absorbed into the system and consequently is far more

harmful than the average person's moderate smoking Raymond Pearl, one of the greatest investigators of longevity has noted that *one of every five heavy smokers* between the ages of thirty and fifty dies before his time [14]

While a minute quantity of concentrated nicotine is fatal (in solution, for example, nicotine is used as an insecticide), the amount in tobacco smoke is negligible It is the tars and acids in the smoke that are harmful We suggest that our readers try some of the denicotinized cigarettes that are on the market You will find, we believe, that they produce even more tongue bite than ordinary, untreated cigarettes In our opinion such removal of nicotine is of negligible value

The caffeine in ordinary coffee and other caffeineated beverages, however, is completely absorbed by the body, and consequently all such drinks should be avoided

The proof of any diet is in the eating Both of these diets have proved to be eminently successful in the treatment of patients with low blood sugar induced by overactive islands of Langerhans Both avoid or, in Dr Portis', correct for foods which would induce a sudden rise in blood sugar and thus stimulate the islands of Langerhans, and both provide the correct food frequently enough to level off the drops that tend to follow meals

A generation ago, Americans sat down to breakfasts which continental Europeans considered monstrous The British have always been hearty eaters Perhaps Americans on the farms, in villages, and in small towns still eat those old time breakfasts We don't know We are city dwellers But we do know that in urban areas and industrial areas among the multitude who "go to work"—and that is overwhelmingly the largest part of the population—a decent breakfast fit to cement body and mind together with sufficient blood sugar is rapidly becoming extinct Many a young female careerist considers black coffee and cigarettes the proper way to break a

twelve-hour fast and equip herself for the morning's work The office worker doing this only slows the wheels of commerce in addition to injuring her health The industrial worker also causes accidents Dr Portis has written about the relation between fatigue states and industrial accidents and has shown that a good breakfast and frequent feedings throughout the day are essential to the prevention of accidents

"A canvas of 50 000 students from first grade through college revealed the startling fact that 65 per cent habitually ate a breakfast entirely inadequate for their physical needs and 16 per cent ate no breakfast at all" [15] The result is the inattention and poor scholarship of which present-day teachers complain 'Army efficiency engineers, investigating almost 1000 accident cases in ordnance depots, recently found that a large majority of the injured workers had come to their jobs without breakfast, resulting fatigue and carelessness had struck them down" [16]

According to Dr E V McCollum of Johns Hopkins University, "hidden hunger" is a pernicious malady *Hidden hunger* is indeed an apt description of the vague discomfort that afflicts the fatigue patient who, though unaware of it, is as in need of food as the ravenously hungry victim of a more pronounced hyperinsulinism [17]

That hackneyed expression, "the tired businessman," is not merely a humorous quip but the simple truth The executive group comprising the managers of our large corporations are so fatigued that they are dying at a rate in excess of, and an age that is younger than that of the general population During the decade from 1940 to the present time industry has come to recognize that the toll of death and disability in the management group is excessive" In 1944 General Motors reported that one hundred and eighty nine of the corporation's management group had died in the preceding five years [18]

"The Life Extension Institute reported that of 1000 holders of life insurance policies in amounts of $25,000 or over who had received extensive examination since January 1, 1938 79 per cent were found to have physical impairments (18 5 per cent of which were high blood pressure and 22 per cent abnormalities of the heart)" In May, 1950, Dr S C Franco reported finding major disease in 25 per cent of all executives receiving periodic health examinations [19] Finally, *Fortune* in an article, "Why Executives Drop Dead," quoted the Life Extension Examiners of New York to the effect that "60 per cent of the executive group examined had conditions requiring a physician's attention, the larger part of them of a cardiovascular nature" [20] It has remained for Dr Sidney A Portis to call attention to conditions among younger executives that "if permitted to go unrecognized, may produce morbidity and mortality of a degree similar to that already reported" [21]

In a paper read before the Section on Preventive and Industrial Medicine and Public Health at the Ninety ninth Annual Session of the American Medical Association in San Francisco on June 29, 1950,[22] Dr Portis stated that exhaustion in relatively young executives "has not been stressed by other investigators in surveys previously published" For many years Dr Portis has been seeing "executives in their early forties and fifties who became utterly exhausted" He made a study of fifty such executive patients all under the age of fifty, and he discovered that 'in 60 per cent of the group fatigue was one of the outstanding complaints" He subjected these business executives to the three-hour Dextrose Tolerance Test 'In 58 per cent of the entire group of executive patients, the third-hour blood sugar level was below the initial level determined during fasting In some instances there was a drop of 30 to 40 mg per 100 cc, while in others the drop was between 5 and 15 mg One severely fatigued executive showed

a fasting level of 87 mg per 100 cc" which is not below normal, but "at the third hour his blood sugar level had dropped to 44 mg"

In previous studies Dr Portis has shown that this relatively low blood sugar is due to an overstimulation of the islands of Langerhans—hyperinsulinism—"mediated by the parasympathetic nervous system via the vagi Blocking of the vagus nerves with atropine sulfate throughout the twenty four-hour period has resulted in the elimination of this drop in blood sugar values Several patients who have had a vagectomy for treatment of peptic ulcer have also shown a diminution of their drop in blood sugar values

Dr Portis' studies have shown that when the amount of sugar circulating in the blood is inadequate, 'the brain does not function properly, the patient becomes high strung and easily fatigued, and the body does not maintain its competence" An almost constant feature in the life situations of the tired young businessmen whom Dr Portis treated 'was a loss of zest, loss of enthusiasm,' and the replacement of such beneficial emotions with boredom and antipathy for their jobs, business superiors, and associates"

He tells us that psychological studies have revealed that "as a rule" the executives who develop these physical symptoms of fatigue are "dependent men whose insecurities and feelings of inferiority are great This intense fear of being found inadequate, rather than real joy in their work, is the driving force of insatiable ambition The machine of the body is being driven by a lean mixture, by the wrong kind of mixture The result is injury that reveals itself eventually 'in symptoms in the gastrointestinal, cardiovascular, respiratory, and neuro-muscular systems"

On the surface these executives appear to get along with each other But "their relations to their families are frequently hostile, so that their wives and children are injured Frenzy

hausted when he came home at the end of the day His wife was struggling along with three children and no diversification in her day's work When she would have liked a break in the monotony of her domestic life, she found that her young husband was content to sit around and recover from the fatigue of his daily efforts in the plant This furnished a desirable escape mechanism for him The situation was aggravated by lack of adequate social outlets, since the couple could not become too closely associated with the younger executives because of the danger that such personal relations would be detrimental to efficiency in business

Analysis of this executive's life situations showed him to have the aggressive, dependent type of personality commonly seen among executives The patient s mother had died when he was 9 years of age, and he had been passed from one relative to another until his father remarried two years later He had been a football player and had subsequently married had three children and become successful, rising to be executive director of a plant employing 400 workers The onset of his complaint coincided with the development of a fatigue syndrome in his wife, who was distinctly bored and unhappy with life in a small town and who complained bitterly of the lack of social and intellectual diversion

What does all this add up to? On the one hand the business of the plant was conducted more efficiently and production costs were lower than in its previous location On the other hand, at the end of five years its top executives were distinctly bored and tired and sooner or later became inefficient Of course management and business must get a fair return on their capital investments or they will not be able to enlarge, modernize or expand their plants But business should realize that highly developed highly skilled workers must have some chance for diversion in their life outside the plant This may mean that management may not profitably locate plants in areas where the labor market is good if the price they have to pay is a breakdown in the efficiency of their top executives

Fifty-five executives under the age of fifty were referred to Dr. Portis by various corporations for "prophylactic examination" These were not men who considered themselves ill, nor were they sent to him because someone else thought so They were sent for a check up They were given a complete physical examination including such laboratory tests as urine and stool analyses, complete serologic study, blood counts with differential, electrocardiogram, 2-meter roentgenogram of the chest to determine the exact size of the heart and condition of the lungs and determination of the basal metabolic rate" In addition, each man was interviewed concerning his previous clinical history and also what may be called his social history his childhood, education, family, environment, jobs previously held and reasons for leaving, marital status, home life, friends, vacations, relations to his superiors, equals, and those under him—in short, everything that could be found out about him

Dr Portis reports that the average businessman does not go to the doctor of his own accord Of these fifty five who had been sent to him, twenty-eight or 50 5 per cent had not had a physical examination in two years Another 27 3 per cent had not had one in five years Yet "only 5 4 per cent of these men were considered entirely normal without any physical defect" Some 29 1 per cent had hypertension, 27 4 per cent had obesity The electrocardiograph showed abnormalities in 12 7 per cent, and another 10 9 per cent on the borderline of abnormality Of these men who thought themselves well, 10 9 per cent had fatigue, as compared with 60 per cent of those who had gone to the doctor of their own accord because they knew they were sick The survey "revealed two important facts first the lack of adequate medical study prior to this study, and second, the high incidence of asymptomatic organic disease"—diseases of the cardiovascular system which are without symptoms Dr Portis concludes that the average

man or woman 'thinks his or her organs are superior, although he knows less about the workings of the human body than he does about an automobile He does not take into consideration the fact that, although one can get new parts for an automobile, no new parts have been developed for the human machine at the present writing The intelligent person who has an automobile will take that machine into a service station every one or two thousand miles to have it oiled, greased, and checked, but he does not give equivalent care to his own body"

By now we have reached a phase in the development of the concept which enables us to clarify some of the uncertainties with which we were confronted To return to the classification of the disorders of the islands of Langerhans, we have, in the descending order of severity

1 Malignant insulomas
2 Benign insulomas
3 Functional hyperinsulinism

Now, the latter group can be subdivided into

a Manifest hyperinsulinism
b Subclinical hyperinsulinism

In manifest hyperinsulinism the classical (if such a term can be applied to a condition of so recent discovery) symptoms of hyperinsulinism, such as rabid hunger, faintness, etc come to the fore In subclinical hyperinsulinism the degree of lowering of the blood sugar is so slight that the usual symptoms of the disturbance are wanting While the normal blood sugar is around 140 mg per 100 cc, in the subclinical hyperinsulinism state it hovers around 80 or even lower Thus, the victim of this abnormality suffers from a chronic partial glucose starvation He feels more or less as normal people do if they go without food for several hours His human machine is being run on a lean mixture Since sugar is the chief fuel for

all the activities of the body, the effect will be felt throughout the body Local conditions will determine exactly which part or function of the body will be most affected which is why hyperinsulinism can produce such variegated symptoms And this is also why it has failed to be recognized so often We submit that it is a most widespread condition because of the excessive consumption of caffeine in the United States One thing is certain—it is far more common than its opposite, diabetes

6

Alcohol and Alcoholics

ALCOHOL, STIMULANT OR DEPRESSANT? —COMPULSIVE DRINKING—THE "PROBLEM DRINKER"—ALCOHOLICS ANONYMOUS—ALCOHOLISM, DIABETES, AND HYPERINSULINISM—MORE CASE HISTORIES

THERE HAVE BEEN drinks, drinkers, and drunks on earth since long before the dawn of history The custom of drinking alcoholic beverages must be at least thirty thousand years old Wine and beer making are probably man's oldest arts In spite of this antiquity, we still do not know why a majority can drink without getting habitually drunk and a minority cannot Though there are many theories, there is no one, officially accepted, scientific hypothesis to explain alcoholism

This is largely because scientific knowledge of alcohol has come to us belatedly Primitive men thought that these exhilarating beverages were a gift from the gods, and they called whatever it was in them that made them that way, 'spirits" At first they drank these beverages communally and ceremonially With appropriate rituals, incantations by priests and medicine men, dancing by maidens and youths, and recita-

America where most of it now is grown in Brazil and consumed in the United States

The alcohol problem never had a chance once the Puritans got hold of it It was inevitable that science would be excluded from its consideration until the moral utopians had had their day To paraphrase Winston Churchill, never before had a well meaning few done so much harm to so many as in the noble experiment of Prohibition It set us back at least a generation Quite apart from its enormous by products of social evil, it perpetuated the point of view expressed by William Graham Sumner when he said, 'If a drunkard is in the gutter, that is where he belongs," and added to it, "until a policeman comes along and carries him off to jail."

It wasn t until after Repeal and the descrediting of the moralist point of view that science was at last able and encouraged to take a hand Perhaps science which had given us the miracles of our modern age would succeed with alcoholics where everything else had failed

The notion that alcoholism is a disease and not a form of moral depravity has long been held among an enlightened minority Even in ancient times there were some who regarded alcoholic intoxication as a form of temporary insanity *In* Sanskrit for example, the word for alcoholic intoxication and for insanity is the same But widespread acceptance of the idea, that alcoholism is a disease like any other noncommunicable disease has come in this country only since Repeal and especially in the last fifteen years In that time, however, mostly in the decade 1940–50, a revolution has taken place in public thinking concerning alcoholism Science has come up with nearly all the answers except one As C Lester Walker has aptly expressed it [1] We are still trying to find out what puts the drunkard in the gutter in the first place, *but we no* longer feel that, once there, it is the inevitable or proper place for him " And once rid of the idea that the only way to prevent *some* people from getting drunk was to prohibit *all* people

from drinking, only then did we begin to make real progress toward solution of the problem.

Just how much of a problem is it? Of the current estimate of sixty-five million drinkers of alcoholic beverages in the United States, some four million are alcoholics, according to Yale University's famed Section on Alcoholic Studies of the Laboratory of Applied Physiology. "This means that there are probably 20,000,000 people, nonalcoholics among whom these alcoholics live and have their being, who are more or less seriously affected by the alcoholics' behavior." [2]

The direct and indirect cost to the nation of alcoholism has been estimated by various authorities at between three quarters of a billion and a billion dollars a year. This is a sum large enough to make it worth while to spend at least a quarter of a billion on research for a few years to prevent it. Especially is this advisable in view of the fact that the number of alcoholics in proportion to the total number who drink is increasing all the time. The grand total of the nation's imbibing of alcoholic beverages—in spite of the ravages of Prohibition which taught women to drink as they never had before—is below its peak of two and a half gallons of absolute alcohol a year for every adult. The crest of our drinking was reached between the turn of the century and the beginning of World War I. By 1940 it had declined 40 per cent, but now in 1950 it is 30 per cent higher than a decade ago.

One of the jobs well done by science in the last decade has been to relieve the public mind of its many glaring misconceptions concerning alcohol. Many of these downright lies were fostered by the Prohibitionists—good people who saw nothing wrong in using foul means to attain what they believed was a worthy end. Let us take a brief refresher course in the fundamentals of our scientific knowledge of the subject. To begin with, "The subtle alchemist that in a trice Life's leaden metal into gold transmute," is ethyl alcohol, chemically C_2H_5OH—nothing but oxygen, hydrogen, and carbon. The

same elements are found in sugar, starch, and fats In fact chemically speaking alcohol and water *are related* "*Alcohol* whatever the kind, has an oxygen hydrogen combination called the -OH group, exactly as does water, HOH *Hence* alcohol tends to dissolve in water One might think of water as an alcohol, hydroalcohol 100 per cent pure The kind of alcohol one has depends on the kind of tail one puts on the OH dog Attach CH_3 and the result is methyl or wood alcohol which blinds and kills Attach C_2H_5 and it is ethyl or grain alcohol, the age old consoler of mankind " [3 4]

This substance, ethyl alcohol, is produced in nature by the process called alcoholic fermentation in which the sugar in fruits is changed into alcohol and carbon dioxide by the action of yeast a simple form of plant life which will grow in sugar under the right conditions The spores of this plant are airborne Ethyl alcohol is not a poison like its cousin methyl *alcohol It is a food* Each ounce by weight, of *absolute* alcohol has 210 calories This is exactly the same as a half *pound of sea bass* A *better source of comparison with other* foods is this 1 gram of alcohol yields 7 0 calories, whereas 1 *gram of carbohydrate or protein gives only* 4 1 calories Al cohol is exceeded only by fats which furnish 9 3 calories per gram Like other foods alcohol burns in the body

It is for this reason that a drunk can go for days and even weeks on nothing but alcohol without starving to death No one can flourish on alcohol however because it contains noth ing but calories—no vitamins whatever A lengthy diet of alcoholic beverages will produce only the diseases of vitamin deficiency such as beriberi and pellagra

Drinking in moderation never harmed anyone, and even drinking habitually to excess does not *cause* any of the ills it was once supposed to such as insanity by "*corroding the cells* of the brain —a favorite with the Munchhausens of Prohi bition It *does* not *cause kidney trouble, hardening of the ar* teries, high blood pressure, cancer, or stomach ulcers It may

be *associated*, however, with *ulcer*, but for a reason to be discussed later It does not *cause* cirrhosis of the liver (Mohammedans, who do not drink at all, have more cirrhosis than we do) But there is some association between cirrhosis and alcoholism, probably of a nutritional nature

Drinking does not injure the germ plasm, so that alcoholism cannot be hereditary What *is* inherited is *something* which *predisposes one* toward alcoholism Raymond Pearl found that potential alcoholics seem to run in certain families whose other individual members are usually total abstainers, whereas the "average" family of moderate drinkers seldom if ever tends to produce a drunkard Pearl also showed that both alcoholics and abstainers are shorter lived than average moderate drinkers

One of our most cherished illusions is that alcohol is a stimulant IT IS NOT It does not "pep you up," make you stronger, more clever, or more efficient It is a narcotic, a "descending central nervous system *depressant*" It attacks the highest brain centers first, then works downward through the central nervous system, putting to sleep and paralyzing the areas of the brain that control muscular coordination, speech, sight, and other sensory centers, and finally, the vital centers in the medulla become so impaired that the alcoholic sinks into a stupor, which may end in death by *respiratory paralysis* Alcohol is also the only sedative that will effectively *cure the hang-over jitters of overindulgence in it* As a painkiller it is three times more effective than aspirin Unfortunately, if you take enough alcohol to dull a really bad pain, you are drunk

What alcohol actually does is to create the illusion of stimulation by deadening the critical faculties Alcohol makes you think you are better than you are. It breaks the chains of your inhibitions, freeing your behavior from any consideration of anxiety as to what others will think of you Dulling the mind's pains as well as the body's, erasing anxiety, apprehension,

and worry, alcohol suffuses the whole being with the glow of a wonderful expansiveness The psychologists call it euphoria *While the euphoria lasts,* you are the man of your dreams, only even more so

In several university laboratories psychologists have conducted scientifically controlled tests which definitely prove that people do not function better, even after only a few drinks, than when perfectly sober These tests have shown that the subjects' visual reactions are impaired by one third Their ability to memorize poetry is cut in half Their facility for solving mathematical problems is reduced 13 per cent while their reasoning is subject to 67 per cent more errors Even their muscular strength is decreased by 10 per cent although the subjects are quite sure they feel less fatigued!

There are, however, a very few people whose reactions do improve after a *few* drinks These are the very shy and inhibited persons whose inferiority sense makes them ill at ease and never at their potential best in the presence of others The relaxing and disinhibiting effects of a *few* drinks bring these psychologically subnormal people up to par

In spite of these exceptions and what still may be the reader's personal conviction—based upon the exhilaration felt following a few drinks after a trying day—alcohol actually anesthetizes the drinker as surely as ether But alcohol puts one to sleep slyly and insidiously, as if it were doing the very opposite

What is the composition of alcoholic beverages? The malt liquors—lager beer, ale, porter, and stout—have the lowest alcoholic content about 4 to 4 5 per cent and never over 6 per cent They also have considerable amounts of carbohydrate and very small amounts of protein, but no fat The dry table wines—(red) Burgundy, claret, etc, and (white) sauterne, Rhine, etc—have less carbohydrate and protein and more alcohol about 10 per cent to 12 per cent The fortified wines—sherry, port, madeira—if they are sweet, are highest

in carbohydrate of any alcoholic beverage except the sweet cordials The alcoholic content of the fortified wines is between 15 per cent and 20 per cent The hard liquors—rum, gin, brandy, rye, bourbon, Irish, and Scotch—have no carbohydrate or protein whatever Their alcoholic content varies from 35 per cent in Scotch, rum and gin to 40 per cent in Irish, rye, and bourbon, and 45 per cent in vodka

Now when we drink any of these alcoholic beverages, the carbohydrates (if any) and the negligible amounts of protein (if any) are digested just as in any other foods While the carbohydrate is transformed into glucose, however, the alcohol does a very strange thing It is *osmosed* through the walls of the stomach About 22 per cent seeps right into the blood stream When it gets to the heart it does another strange thing Alcohol is no more a heart stimulant than it is a brain stimulant It does not speed up the heart—it simply releases the controls and permits the heart to act practically as it

first it dulls that part of the brain which censors and inhibits our behavior This sudden relaxation, after the worries, anxieties, and apprehensions to which flesh is heir, gives us that wonderful sense of release An alcoholic once remarked that his idea of heaven would be to dwell eternally in the golden glow of well-being and self-esteem that follows the first drink and is so soon the memory that one tries in vain to recapture

The drinks that follow the first one or two or three steadily increase the concentration of alcohol in the blood The anesthetizing effect moves from one region of the brain to another After the highest centers have been dulled and our judgment destroyed, gradually but inexorably the areas of muscular coordination, speech, and vision are affected We begin to weave a little as we walk We miss the end of our cigarette as we try to light it Our speech becomes thick and slurred,

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sode, and so on, day after day, until his funds are depleted or he lands in a hospital with delirium tremens The hospital gets the alcohol out of his system and he leaves, still a little shaky, but sober For a week or a month he doesn't touch the stuff Then something happens He meets a friend he hasn't seen for years and the happy reunion calls for a celebration Or it is New Year s Eve, or he is invited to a very special cocktail party, or he is passing a bar, and for no apparent reason, he goes in to have "one—just one" Invariably the cycle of intoxication and hang over is reinitiated

What enslaves the alcoholic to a liquid which others can manage with pleasure and sometimes even profit? What compulsion relentlessly drives him to his own destruction? His family and friends implore him to stop drinking—in vain Repeatedly he himself pauses to scream his abject shame and remorse Surely there is no other disease like alcoholism What causes it? How can it be cured?

While there is no officially accepted hypothesis to account for alcoholism, several have been submitted They fall into three main categories the psychological, the physiological, and a combination of the two Once it was admitted that alcoholism was a disease and not a perverse moral depravity, the psychiatrists the psychologists and the psychoanalysts moved in and took over This malady, so unlike any other, more akin to neurotic and psychotic states, surely was a mental and not a physical disease, and, as such, their province

Under the lingering influence of the Freudians, the "flight-from reality' hypothesis was most frequently ascribed to the alcoholic He was running away from life seeking nepenthe in alcohol Why? Because—but now the psychological school spread out like an umbrella tree He was running away from life because he was a rejected child Unwanted and unloved, he recoiled from life He was running away from life because he was a spoiled only child on whom his parents, especially his mother, had lavished so much love and devotion that the

our vision is blurred and eventually doubled Sooner or later, as the higher faculties that make us human are all put to sleep, we become animals And finally, when the alcohol con centration in the blood reaches about ten ounces, we "pass out"

As we all know from observation, the pattern of intoxica tion varies enormously from person to person These variations have been corroborated by studies Seven per cent of a thou sand drinkers were still sober with a 4 per cent concentration of alcohol in the blood Ten and a half per cent were intoxi cated with a concentration of only 05 per cent, or eight times less In addition, there are factors apart from individual idio-syncrasy *One can drink a great deal more without becoming* intoxicated, for example, if there is food in the stomach to absorb some of the alcohol

Alcohol also increases the peripheral, or outside, circulation by which the nerves are fed This would be beneficial but for the fact that as our drinks 'wear off," the nerves are sealed [illegible] This is what makes a [illegible] sides depleting the body's vitamin B content, essential to the nerves, the alcohol also seals up the lifelines of the fuel supply, the peripheral circulation And only alcohol itself will re open them This is why, until very recently, there was nothing but alcohol to assuage a hang over Today there is another remedy (which we shall discuss later), but it cannot be carried about as con veniently as an aspirin, or administered as easily as a few ounces of whisky

A normal man may get drunk and suffer a hang over *He* tapers it off with "a hair of the dog that bit him"—a little *liquor By the next day he is a well man,* his spree but a mem ory He may not get drunk again for weeks, months, a year, or ever The alcoholic however, usually cannot get by the hang over of the "morning after" In curing it, he does more than simply taper off—he involves himself in a new drunken epi

of greatness How often you hear it said of him if only he would quit drinking he d be at the top

"Early in his quest for the more abundant life the alcoholic discovers alcohol On his first sizable drink of this elixir he experiences a high surge of feeling a strong exaltation 'This is it This is the life for which you have been seeking This is Truth and Good This is a glimpse of eternity It almost says to him 'This is a little bit of God

"And because there is an almost immediate let down because he feels his elation oozing away and he wants desperately to recapture it he calls for another drink This however may give him the lilt of the first drink but in addition it gives him a further let down so trying vainly to re glimpse eternity, he orders a third and a fourth and a fifth until he is unable to feel anything at all—at least for some time

The alcoholic does not often see clearly that he is looking for life Too often he is told that he is running away from life —from what people are pleased to call *reality* Eminent psychiatrists even tell it to him But the inner voice continues to say that it isn t so Consequently he becomes utterly confused and bewildered or cynically skeptical of the opinions of all non alcoholics or again even surly and resentful of them

"In the process he may act the greatest Hamlet of his generation [John Barrymore] write many of the best works of fiction [Thomas Wolfe] or publish them [Horace Liveright] but little by little slowly and inexorably his life becomes unmanageable His intellect and his will are no longer the captains of his soul It is ethyl alcohol who rules At last there may come the realization that he cannot find his happiness in alcohol In his remorse he screams this is *not* it This is *not* Truth *not* Good *not* the more abundant life for which I am looking But he is powerless to do anything about it The throne of his intellect and will has been usurped by a cruel tyrant who

grown man was emotionally still a child Life frightened him so he ran away from it He sought to escape from life because it had become unbearable He had a neurosis, a personality dis turbance resulting from the fact that his beloved had jilted him, or married him and shattered his illusions about her Or he had wanted to be a poet or an artist and had been forced by his father to go into the insurance business He had wanted to be a composer, he had been forced to become a salesman So he drank to hear the music he no longer heard at any other time *Etcetera, etcetera, ad infinitum*

It was a great hypothesis It filled the coffers of the psychoanalysts probing for that hidden motive The one about the spoiled only son almost made off with the band wagon Statistics had buttressed it with respectability *Only sons were (and are) more likely to become drunkards than other men* There was, however, one fly in the psychological ointment Even with the alcoholic's hidden motive removed, the victim of it still could not drink normally After one drink he slipped right back into his ancient ways That wise and mellow psychiatrist, the late Dr Myerson, pronounced the hypothesis "inadequate"

A Roman Catholic priest, who has had vast experience with alcoholics, advanced an engaging hypothesis 'The alcoholic is not running away from life, he is seeking it, seeking it more abundantly The typical alcoholic is not an inferior, but a superior person He has a great driving force, a desire and a yearning for a more abundant life The typical alcoholic is an extremist, a perfectionist He works harder and plays harder than his normal friends Physically, your alcoholic must be more full of life than the average or he couldn t take the beating he gives himself Mentally, he is also usually better equipped than his non alcoholic fellows No matter what his occupation, you will find him near the top He is nearly always someone who starts out with brilliant promise

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holds him in the bondage of a vicious circle of physical allergy and mental obsession, of hang-over, bender, and hang-over, from which he cannot escape except in madness or death "[5]

Outstanding in the field of psychologists who have devoted themselves to the study and treatment of alcoholism is Dr (PH D) Charles H Durfee Perhaps more than anyone else, he has taken a purely objective, scientific attitude toward the subject, unprejudiced by any conceptions from the past He has collected an enormous amount of data, almost entirely the result of his own experience with alcoholics, and has de veloped an eminently successful method of treatment based on this material Dr Durfee believes that "drinkers are made not born ' While recognizing the existence of inherited and environmental predispositions, he believes that "excessive *drinking is essentially a learned, inadequate way of reacting* to personality difficulties—that drinking habits are acquired Their correction, therefore, can be brought about only through a process of unlearning and re education '[6]

Dr Durfee is quite certain that there is not merely *one* "al coholic type " The neurotic, who is fearful of life and running away from it, is one of many different kinds of people with different personality difficulties who may resort to alcohol "No one is born an alcoholic and there is no such thing as an alcoholic type There are only individuals who drink for vari ous reasons "[7] In another place he wrote, "many excessive drinkers are otherwise well adjusted people . . Such drink *ers have learned to drink through drinking* "

Inasmuch as alcohol is not a habit forming drug (in the same sense as, for example, morphine or cocaine), it may seem strange that the alcoholic apparently has such an ir resistible craving for it This craving is physiological only as long as alcohol remains in his system Once the last of it has been removed by oxidation, no physiological craving re mains According to Dr Durfee, "The force of psychological

habituation, however, cannot be lightly discounted "[8] Elsewhere he wrote, "Psychological habituation is a significant factor in the drinking history of both the maladjusted personality and the normal person More than any other causative element, routine drinking can make alcohol, a drug not physiologically addictive the object of irresistible craving We all know how disturbing even minor dislocations of routine can be—failing to get one's coffee or morning paper at breakfast, or missing a train Alcohol, more intimately related to subjective and physical states such as worry, depression and fatigue, is particularly suited to become a habit especially if indulged in as a regular practice over a period of years To psychological habituation must be added an acquired tolerance, so that increased quantities are necessary to produce the desired effect "[9] The desired effect, of course, is that feeling of lift and glow and release from worry, depression, and fatigue for which the alcoholic drink is taken

Whether or not one can agree with Dr Durfee's dictum that "the foundations of alcoholism are predominantly psychological," one cannot but be enormously grateful for the wealth of fact he has gathered and used to illuminate the physiological and psychological factors

Among his many contributions to our knowledge of alcoholism is the remarkable list of signs and symptoms of what constitutes a "problem drinker," a phrase coined by Dr Durfee and which he uses in preference to alcoholic Some critics of Dr Durfee aver that "problem drinker" is a Victorianesque euphemism for an economic elite which cannot stomach the harsh truth of "alcoholic" This is not the case Dr Durfee expla [illegible]
in soc [illegible]
Ther [illegible]
believe that no stigma should be attached to the term Every effort should be made to point out the patent absurdity and ignorance of such a stigma in dealing with a disease For

just as the diabetic cannot live without insulin so the alcoholic cannot live with alcohol

Dr Durfee s reasons for coining the term problem drinker rather than bucking the current were motivated by therapeutic experience He found in treatment of alcoholics" that this suggestion of weakness and moral unfitness may do serious psychological harm to patient and therapist alike in discussing the problems posed by alcohol Dr Durfee defines the problem drinker as a person in whose life drink over shadows threatens or has already destroyed what we consider normal living

The first of Dr Durfee s eight signs and symptoms is "to draw a blank —that not uncommon experience in which after a certain number of drinks the drinker is intoxicated but maintains consciousness apparently aware of what he is saying and doing only to remember nothing whatever of what he has *said or done the next day* This *occurrence is a definite sign* of physiological changes taking place within the drinker

Dr Durfee calls the second sign extra curricular drinks This takes many forms such as pantry drinking" at parties feeling the need for "a quick one before the party or the meeting or feeling that the drinks are too weak or served with too great an interval between them These are all indications of the incipient problem drinker

The third sign is an unwillingness to talk about liquor as a problem in his life and a readiness to accuse friends and family

The this takes

the for a drink

When rationalization is carried over from justifying a few drinks to justifying a succession of drinks with no considerable period of abstinence then the familiar mental pattern of the problem drinker has taken shape "

t

alcohol has lost its true relative value to its victim" At this stage 'the prospect of a drink is more pleasing than any other aspect of a party, a conference, a day or an hour of relax ation"

The sixth item, "change in the character of hang-overs," is momentous On the "morning after," an ordinary heavy drinker has "a headache and marked fatigue A chronic drinker's hang-overs, however, are like no other ailment known to man" In addition to such physical symptoms as extreme fatigue, with acute muscular pains, excruciating headache, butterflies in the chest, nausea, and belching, he is the prey of such psychological symptoms as "morbid apprehension, vague but inescapable fears, feelings of guilt and shame He is about as thoroughly miserable as a human being can be" The things that used to mitigate his earlier hang overs—'aspirin, black coffee, and fruit juices—" are of no use now "Alcohol alone will temporarily bring relief As the day progresses he will have to maintain a steady intake in order to feel normal By nightfall he has a heavy concentration of alcohol in his bloodstream and is apt to end up in a rotation of maudlin, bitter, and unenjoyed drunkenness After long years of drinking [other authorities specify an average of fifteen years for a man and ten for a woman], one of his sprees may culminate in delirium tremens or acute alcoholic hallucinosis"

Gastrointestinal disorders are the seventh group of signs and symptoms 'This is indicated by a failing appetite, particularly at the beginning of the day" As for the morning tremors and other hang over symptoms, the alcoholic's cure for this is the eye opener, so that "he eats less and less, until alcohol becomes both food and drink to him The result is a vitamin deficiency found in most excessive drinkers"

The eighth and final item on Dr Durfee's list consists of two conditions—insomnia and irritability—"characteristic of the problem drinker," which "may have serious consequences psychologically both for himself and for his family." He con-

had only one or two slips or slide backs" The remaining 25 per cent have stumbled out of the ranks of sobriety more than three times but the vast majority are still struggling to keep up with the band wagon

What is the secret of this enormous success? Not all these men and women have had theophanies Most of them have never even heard of their founder s experience (To our knowledge this experience has been published only twice before)

These are the elements of which that success is built Alcoholics Anonymous is not tied to either the physiological or the psychological "school" of causation In the opinion of the late Dr William Duncan Silkworth once Physician in Charge of the A A Wing in Knickerbocker Hospital New York City alcoholism is due primarily to a physical allergy but also to a "mental obsession" Alcoholics Anonymous is composed entirely of alcoholics who refer to themselves as such whenever they introduce themselves at an A A meeting This gives the newcomer a measure of sympathetic understanding without censure or coddling that he could not possibly obtain from anyone but another alcoholic who knows from personal experience everything he is undergoing

He is given Twelve Steps to study and to practice Printed on a small card to be carried in his pocket they are the blue print of a way of life which is essentially Christian Indeed [illegible] find them rem[illegible]scent of *The Spiritual* [illegible] of course neither the [illegible] who together wrote the Twelve Steps could conceivably have read *The Exercises* These are the Twelve Steps

1. We admitted we were powerless over alcohol—*that our* lives had become unmanageable
2. Came to believe that a Power greater than ourselves could restore us to sanity

3 Made a decision to turn our will and our lives over to the care of God *as we understand Him*
4 Made a searching and fearless moral inventory of ourselves
5 Admitted to God, to ourselves, and to another human being the exact nature of our wrongs
6 Were entirely ready to have God remove all these defects of character
7 Humbly asked Him to remove our shortcomings
8 Made a list of all persons we had harmed, and became willing to make amends to them all
9 Made direct amends to such people whenever possible, except when to do so would injure them or others
10 Continued to take personal inventory and when we were wrong promptly admitted it
11 Sought through prayer and meditation to improve our conscious contact with God *as we understood Him* praying only for knowledge of His will for us and the power to carry that out
12 Having had a spiritual awakening as a result of these steps we tried to carry this message to alcoholics, and to practice these principles in all our affairs

In the twelfth step the new Alcoholics Anonymous member becomes the guide, sponsor, and counselor of a newer A A member So the good work is carried forward in an ever-widening circle

What A A has put into successful practice is essentially a cure by *faith* similar to the many individual cases to which the late Dr Alexis Carrel testified to the astonishment of his medical colleagues Science is baffled by the cure by faith, the occurrence of which it can neither deny nor adequately explain Inasmuch as Alcoholics Anonymous is practicing this strange phenomenon upon a mass basis, it should afford some inquiring and not too bigoted minds an opportunity to elicit a rational explanation

"There is another respect in which the work of Alcoholics

Anonymous on behalf of the alcoholic stands apart from that of most other agencies It gives the middle class drunk a break which he has long badly needed In every large city hospital there is an alcoholic ward that saves the lives of and gives temporary rehabilitation to those alkys who were born in or who have sunk to the lowest strata of society In various parts of the country there are exclusive sanatoria where in a country club like atmosphere the rich inebriate can sober up and try to make a fresh start Until the advent of Alcoholics Anonymous the middle class that is the average medium income-bracket alcoholic had no adequate curative agency suitable to his means and social position

Speakers in Alcoholics Anonymous generally preface their remarks with the statement that the ideas they are about to express are their own and do not necessarily represent the views of the group as a whole

It is one of the virtues of Alcoholics Anonymous that by means of this fluid type of organization it has escaped the evils of institutionalism so often inimical to movements for social betterment " [1]

The allergic basis for the physiological explanation of alcoholism is not by any means uniquely held by the medical advisers of Alcoholics Anonymous But the exponents of this view admit that whatever may be behind the allergy is understood no more than any other allergy In explaining the matter Dr Silkworth said It would seem that through some defect probably in the metabolism [italics are ours] "

An echo of these words may be found in C Lester Walker s *Harper s* article already quoted Professor Roger J Williams Director of the Biochemical Institute at the University of Texas is a leading exponent of this idea [the metabolic] He pointed out how often our metabolism differs from person to person in actual operating detail

Last year William L Laurence science reporter of *The*

New York Times reported on the work being done by two different medical groups in New York City He calls it "the glandular treatment for alcoholism [which] was first reported on over a year ago by Dr John W Tintera, chief of the Endocrine Clinic, St John's Riverside Hospital, Yonkers, New York, and Dr Harold W Lovell of the New York Hospital and New York Medical College before the annual meeting of the American Geriatrics Society at Atlantic City" A more recent report —May, 1950—was made to the annual meeting of the Medical Society of the State of New York by Dr James J Smith, director of Research on Alcoholism at the New York University–Bellevue Medical Center Both groups working independently, as often happens, had arrived at almost identical conclusions

Alcoholism is caused by a deficiency in the adrenal cortical hormones—those hormones whose action is antithetical to insulin The trouble may not be in the adrenal cortical itself, however, but in the master gland, the pituitary, which for some reason fails to stimulate the adrenal cortical glands as it does in normal operation of the endocrine system It is believed, moreover, that this disability of the pituitary is not caused by the alcoholism but antedates its development What is certain is that injections of ACTH, ACE, and cortisone have had a miraculous effect on drunks, even at their very worst, sobering them up with practically no hang over within twenty four hours of administration [13]

These spectacular "cures" are a great step forward, and they provide evidence in reverse for the theory which the medical and the lay members of this collaboration arrived at independently that hyperinsulinism with its chronic partial blood sugar starvation is an essential underlying condition of alcoholism

To the lay writer it was just a bright idea to be discussed with anyone who would listen, especially with the many who

knew a great deal more about alcoholism than he Naturally, he discussed it with the medical collaborator and immediately learned that the latter had been doing more than merely thinking about it.

Looking back over twenty years as a diabetes specialist he could not recall a single case of a diabetic who was also an alcoholic Could it be that like the allergies—hay fever, asthma, rheumatic fever, and peptic ulcer—alcoholism also *was one of those strange ailments associated with the low* blood sugar of hyperinsulinism? Many factors pointed to the possibility The reader may recall that those seeking a physiological rather than a psychological cause for alcoholism have pondered the possibility of allergy and metabolic imbalance *He may be impressed (as we were) by the strange similarity* of many of the symptoms of alcoholism in its hang over stages and of hyperinsulinism in its most definite forms He may wonder if the alcoholic s strange craving for a nonaddictive drug *may not be* a craving for sugar, developed because the imme*diate effect upon the body of a dose of alcohol is similar to* that of a dose of pure sugar Thus the alcoholic, not realizing he is sugar starved takes this erroneous way to stifle the pangs of a desire whose true origins he does not understand In the *course* of recent practice the medical collaborator confirmed *this hypothesis by the results of the Glucose* Tolerance Test on alcoholics who came to him

J M is a highly successful New York lawyer His quick mind and highly keyed personality give him a decided advantage over slower witted adversaries As a trial counsel in civil suits he has won *fabulous verdicts* The less spectacular and perhaps more scholarly branches of the law are repugnant to his temperament He leaves them to the *briefers* He enjoys matching wits with opposing counsel in the arena of the courtroom

One day he noticed that he was not up to his usual brilliance He found himself overlooking opportunities to raise

objections and make remarks that would influence the jurors He could hardly wait for the noon recess He needed "a shot in the arm" so very badly! Finally his unuttered prayer was answered The court recessed for luncheon

The lawyer rushed out of the courtroom to the nearest café and ordered a 'double Scotch on the double" As soon as the potion had passed his lips, he began to feel a little better He knew the grateful warmth would course through his body in a few minutes and this knowledge made him less tense He ordered another drink and another and another, until he became almost paralyzed with drink Naturally he could not go on with the case, which had to be adjourned because of "illness of counsel"

On another occasion he developed the "awful thirst" toward the end of the day Fortunately his associates were able to avert a legal tragedy (for the client) by taking him to a steam bath where they kept him all night to "boil him out" The next day he was able to go on with the case

Similar episodes occurred with increasing frequency The story began to get around and his practice to fall off Too many cases were lost because he went to pieces at the crucial time He was still capable of handling a short case, but when the issues were involved and many witnesses had to be examined and cross examined, he simply could not remain sober long enough to complete his work Eventually he began to drink as soon as he got up in the morning An ounce of milk furnishes 20 calories An ounce of 100-proof whisky yields 100 calories As his alcoholic consumption increased, he ate less of other foods His life became a perpetual lost week end

He tried Alcoholics Anonymous, but their methods would not succeed with a man of his skeptical and analytical mind This is not said in disparagement of the very great work that A A does There are some, however, to whom the appeal would seem "revivalist" This sophisticated and cerebrating lawyer could not bring himself to "hit the sawdust trail"

He went to psychiatrist after psychiatrist He knew them *all too well* He had put so many through his brilliant cross examinations He knew all the answers himself and could not *be influenced by others* He had been using suggestion on jurors for so many years that he was immune to it He even went so far as to try hypnosis, but his mind was not amenable He could never subject his will to another's He could never forget to think for himself

Finally a Glucose Tolerance Test was made—not because there was any particular indication for it, but because all other tests in general use had been performed without shedding any light on his compulsion The test revealed that he had hyperinsulinism

It was felt that his "thirst" was a cry for nourishment from *his sugar-starved body* The patient was given the diet His doctor made no reference to stopping drink In three days the patient noticed that he no longer craved alcohol as much as before He still drank, but that almost mad desire which formerly had come over him suddenly was gone He found now that he could 'take it or leave it" After a while he realized that liquor was not doing anything for him He no longer needed its "lift" Being a sensible man, he stopped liquor completely without any outside suggestion

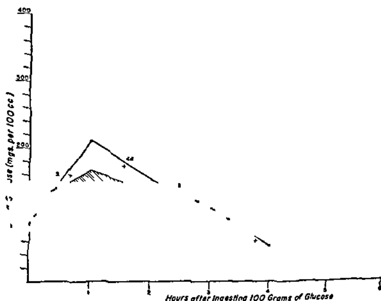
In retrospect, it is easy to understand why he drank. In the beginning he had generally fortified himself against a tough legal battle by drinking several cups of black coffee Coffee does stimulate the brain and make quick thinking easier But the coffee's repeated stimulation of his islands of Langerhans had made them so sensitive that his blood sugar was forced down a few hours later, and he had a sinking sensation that led him to crave some further stimulation The timing of his "binges' lends credence to this explanation After dietary treatment had normalized his oversensitized islands of Langerhans he no longer felt this need for a drink Of course, he could better have relieved those spells of gone" feelings with

something to eat, but like too many people he believed that alcohol is a stimulant The first stiff drink he took made him feel well by robbing him of the awareness of his difficulties How natural then that he should want another to complete the job of restoration of his faculties He could hardly deny the desire for a third and so the vicious circle was established Whenever he needed a boost the whisky bottle was at hand He did not have the knowledge of his own body to know that he was really hungry And in order to sober up quickly after a "binge," he would drink prodigious quantities of black coffee, which only spurred on the underlying trouble

Another case is that of a man of thirty who had learned to take a drink while on combat duty as a bombardier in World War II On his last mission the two right engines were put out of commission and the plane limped back to base When it landed, the landing gear stuck, and the engines were driven back into the cockpit killing the pilot and severely injuring the bombardier He was invalided out of the service, and it was several years before he overcame the horror of that final experience His family was indulgent with him and did not raise any serious objection whenever he took a drink "to steady his nerves" Gradually his alcoholic consumption mounted He ate less and consumed great amounts of coffee He had "the shakes" His hand trembled as he poured out his morning libation His family frantically urged him to give up drink, but they could do nothing with him His liver became enlarged and it was feared that he might be developing cirrhosis of the liver

One day, while he was visiting his parents he suddenly went into a stupor He had not been drinking at all that day Examination revealed an odor of acetone on his breath He was given an injection of glucose intravenously and he soon revived A few days later his mother telephoned the physician that she had attempted to reach her son by telephone and that his failure to answer made her fear that he had again col

lapsed She went with the doctor to her son's apartment They found him still conscious but so drowsy that he had left his office and come home to sleep His mother thought he was drunk, but the doctor again noticed that the odor on his breath was not spiritous but due to acetone He was roused and told to take a glass of milk every two hours until the next day, when a Glucose Tolerance Test was taken The results are so significant that we give the curve



10—*Alcoholism*

This is obviously a case of dysinsulinism The plus signs below each segment indicate that each urine specimen contained acetone The test was terminated at the end of four hours because the patient went into insulin shock the blood sugar being but 54 mg per 100 cc

At the fourth hour the patient had a convulsion, and glucose had to be administered intravenously He was then *told to* take a small glass of milk every hour throughout the day and the following night

This curve at least for the first three hours is a diabetic curve The patient passed large amounts of sugar and acetone in his urine If the test had not been prolonged the only possible diagnosis would have been diabetes—and of sufficient severity to require insulin But the fourth hour drop proved that it was a case of *dysinsulinism* In all probability the liver had been so badly infiltrated with fat that its glycogen stores were depleted Insulin would have done unmeasurable harm The patient had to be treated for his hyperinsulinism (ignoring the diabetic element) and treatment had to be given for the fatty liver which now fortunately is not an impossible task The young man was put on the Harris diet and in addition treated with large doses of vitamins and with lipotropic substances to aid in the regeneration of the liver This was necessary because of the large amount of fat in the Harris diet His urine was examined every day For four days it was loaded with acetone and sugar On the fifth day there was no more sugar but there was still a slight amount of acetone which persisted for another four days His blood sugar was determined about an hour after luncheon. On the third day of treatment it was 176 mg per 100 cc of blood On the fifth day it was 150 and on the seventh day 138 On the tenth day of treatment it was down to only 100—and that only an hour after a heavy meal! The patient gained eleven pounds in the ten days His appetite was enormous

The young man was permitted to get out of bed. His family and friends came to see him and drinks were served The next day he said that he was surprised that even while watching his guests drink he did not have the slightest desire to join them

At the time this account is being written he is still under treatment The enlarged liver has regressed to its normal size He feels better than he has at any time since the end of the war The vitamin injections have been cut down from daily to twice a week but he is still taking the lipotropic capsules

skeleton The bones of a one hundred and fifty-pound man contain somewhat more than two and a half pounds of calcium, while his blood contains less than five grains Yet this tiny amount of calcium is so important that he could not live without it

Each 100 cubic-centimeter portion of blood contains between 10 and 11 milligrams of calcium The amount in the blood *cells* is negligible, some investigators even reporting that there is none When blood is taken from a vein for analysis, a little potassium oxalate or sodium citrate is added to remove the calcium, and thus prevent the blood from clotting The blood remains fluid, permitting measurement for analysis If calcium is to be determined, however, blood samples can not be treated in this manner The blood must be allowed to clot, and the calcium then determined in the clear fluid—the serum

The calcium in blood serves other functions Some of it is combined with the proteins (albumin and globulin) of the blood Some of it exists in the same form as in any solution of a calcium salt This so called ionic calcium is of the utmost importance in maintaining a smooth action of the nervous system When it is too low, we have a condition known as *tetany*, in which the muscles tend to go into spastic contractions

The electron microscope, which can magnify so many more times than its optical predecessor, has revealed that each cell in the central nervous system has a shell of some calcium compound just within the outer wall [1] When the integrity of this shell is impaired, the cell becomes too irritable [2] This might be compared to the rubber insulation on the terminals in a telephone exchange If that insulation breaks down there is a spread of the electrical impulse, so that when we wish to call a particular number, we find ourselves on a perpetual party line In a more or less similar manner, when the calcium shell is thinned out, the nervous impulses are not channelized

properly and we experience a spread of effect beyond the desired path

Changes ... in shifts ... directly ... demonstrated that hyp... ...inism is accompanied by low serum calcium values[3] These same investigators also showed that these changes in sugar and calcium are accompanied by definite changes in the electroencephalogram—the recording of the electrical changes that continually occur in the brain It should be remembered that the br... tissue ...

In treating any of the myriad manifestations of hyperinsulinism, we are not forced to give special consideration to the serum calcium deficiency The diet will, in time, correct the condition by itself and the serum calcium will rise along with the blood sugar If we administer calcium with the diet, however, the process of recovery is accelerated so that what would take months in the absence of calcium therapy takes but a few weeks[4]

There are other mineral constituents of the blood which vary somewhat with changes in the blood sugar level Their effects are relatively unimportant, however, and need be mentioned only briefly Among these minerals are sodium and potassium The blood serum contains much more sodium than potassium, while the cells contain more potassium than sodium The serum potassium is of ... varies ... calcium ... potassium, it is advisab... persons with any of the different manifestations of hyperinsulinism to avoid excessive use of salt (sodium chloride) Asthmatics, it will be remembered, suffer much more with excessive use of salt Therapeutically, we are not

gerhans It may be that this is an effect of ACTH the adreno tropic hormone, but the final answer must await further in vestigation

If the anterior pituitary lobe becomes enlarged and over active after the attainment of maturity, the growth of the body is no longer symmetrical Certain parts grow enor mously The hands and feet and the lower jaw expand com pletely out of proportion to the rest of the body This con dition is known as *acromegaly* The end result is an exaggera tion of a Primo Carnera whose huge size is evidence of pitui tary overactivity Most acromegalics have diabetes because the insulin apparatus is depressed by the excessive production of the anti insulin anterior pituitary hormone Acromegaly is characterized by periods of activity until, for some unknown reason, the process apparently comes to a halt The diabetes then becomes milder, or may even disappear completely, as the excessive production of the anti insulin factor ceases With an exacerbation of the acromegaly, as indicated by an other spurt in growth of the affected parts, the diabetes be comes more severe

Some patients undergo many alternating phases This con dition occurs as a result of the nonselective quality of the enlarged pituitary, in which all the hormones, rather than a particular one, are made more plentiful

The anti insulin effect of the anterior pituitary is also illus trated by the researches of Houssay, of Buenos Aires[5] He demonstrated that removal of the anterior pituitary increased the sensitivity to insulin in otherwise normal animals In other words a smaller dose of insulin sufficed to produce the same drop in blood sugar that was obtained in an intact animal If the pancreas had been removed previously, the diabetes caused by the extirpation of the islands of Langerhans was rendered less severe when the anterior pituitary was removed When an extract of the anterior pituitary was injected into normal animals, the subsequent injection of insulin had less

effect than it had before the injection of the pituitary extract If the anterior pituitary was first removed and then the pancreas was extirpated, the animal rarely developed diabetes, and then of merely a trivial nature When these Houssay animals, as they have been called, were injected with pituitary extract, they developed diabetes or, if they already had that condition in a mild form, it became extremely severe similar to the normal animals whose pancreases alone had been removed Permanent diabetes has been produced in animals by repeated injection of pituitary extracts [6] If the injections are stopped before the islands of Langerhans are permanently damaged, however, the diabetes disappears If, finally, the pituitary extract is injected together with insulin, diabetes is not produced [7]

The posterior lobe of the pituitary secretes what was formerly believed to be a single hormone, pituitrin, which is manufactured from the pituitary glands of cattle It has been used successfully for the treatment of *diabetes insipidus* It will be remembered that this disease is quite different from diabetes mellitus The urine contains no sugar, and the blood sugar is normal The victim of this disease passes gallons of pale, watery urine each day If he inhales pituitary powder or takes injections of pituitary solution, he can control his disease —but not cure it

Pituitrin is also used very widely in surgery and obstetrics Sometimes, after an operation, for example, there is paralysis of the bowel This "post operative ileus" is treated by injecting pituitrin, which stimulates the smooth (involuntary) muscle coats of the intestines, causing them to contract and expel their contents Having a similar muscular coat, the walls of blood vessels will contract upon pituitrin injection, causing the blood pressure to rise In obstetrics, pituitrin is injected into the new mother after delivery of the infant to shrink the uterus It has been found that these two functions —surgical and obstetrical—are performed by two different

blood sugar In the poorly functioning organism, the swings are much greater

If we wish to correct an imbalance in the involuntary nervous system, we can either depress the overactive part or stimulate the underactive part *We have drugs that can fulfill* these functions Sometimes it is advisable to stimulate one system and depress the opposing one by the simultaneous *administration of two drugs*

There is a disease of the adrenal cortex called Addison's disease, in which there is a deficiency of a cortical hormone —cortin This fortunately rare affliction, which only until recently was invariably fatal, is characterized by extremely low blood sugar levels The blood pressure is very low, salt is lost from the body, and there is marked dehydration The *muscles are exceedingly weak and there is great* emaciation far beyond that accounted for by the loss of water' The victim exhibits a peculiar dark pigmentation of the skin and *mucous membranes, especially around the body orifices* Patients were helped somewhat by being fed large amounts of salt which enabled them to retain more water, but this measure only slightly delayed the inevitable death *With the discovery* of cortin, this dreadful process was prevented[9] The symptoms of this disease resemble somewhat those of hyper insulinism, but Addison's disease is, of course, much more serious and severe

During the past twenty years there has been accelerated interest in the hormones of the adrenal glands For some time it was thought that adrenalin was the only secretion, but, when it was shown that adrenalin came only from the medulla, the cortex was thoroughly investigated in many *laboratories Kendall,* working* at the Mayo Clinic laboratories, isolated six crystalline substances from the adrenal cortex[10] These were designated by the names, Compounds A, B

* Dr Edward C Kendall, who retired from the Mayo Foundation on May 1 1951

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In animal experiments it was demonstrated that removal of the adrenal glands after the pancreas had been extirpated reduced the severity of the artificial diabetes [11] When cortical extracts were administered to these animals, the diabetes again became severe [12] If these cortical extracts were injected into normal animals, the blood sugar rose [13] This parallels Houssay's experiments with the pituitary gland

Because the tiny adrenal cortex could not supply these substances in quantity, attempts were made to prepare them chemically from more plentiful sources Reichstein prepared a substance similar to Kendall s Compound E [14] Kendall himself succeeded in preparing Compound A from desoxycholic acid, which is found in bile [15] Sarett then devised a fairly efficient method to convert Compound A into Compound E,[16] and the commercial manufacture of Compound E finally was begun

The successful preparation of Compound E made front-page copy, and the patent medicine men went into operation A substance in wheat germ oil, called *vitamin* E has one definitely proven effect without it rats are sterile No other effects of vitamin E have been definitely demonstrated, although it has been peddled for various conditions on which it has no effect After the press published the startling accounts of the effectiveness of *Compound* E for certain conditions, the sales of *vitamin* E (which in no way is connected with Compound E) rose sharply One company advertised "Vitamin E Compound' [17] To protect the public from such advertising Kendall coined the name "cortisone," which he derived by combining some of the letters in its chemical name, 11-dehydro-17-hydroxyCORTICOSTERONE [18]

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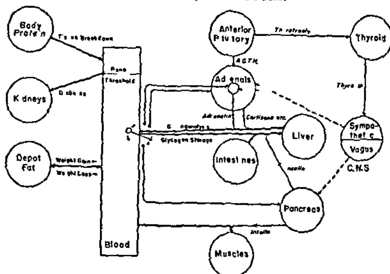
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11—*The Principal Influences on the Blood Sugar Level*

This schematic diagram shows the principal hormonal, metabolic and nervous mechanisms which regulate the level of the glucose in the blood The fine lines indicate hormonal effects and the direction of the influence The heavy lines indicate movements of glucose The broken lines indicate effects from and on the sympathetic and para sympathetic (vagus) nervous systems. The hormones are represented in italics

The small float indicates the effect of changes in the blood sugar level. *When the float rises the pancreas is stimulated to secrete in* sulin when it falls the adrenal cortical hormones are secreted A rapid or profound fall also stimulates the production of adrenalin. These hormonal effects then tend to restore the blood sugar level to its optimal value In addition to its nutritive action glucose in a way, thus acts as a hormone

When enough of the new material was available, Hench and his assistants at the Mayo Clinic tried it in treating rheuma toid arthritis, a crippling condition in which the joints are swollen, tender, stiff, and painful to pressure In addition, the muscles pulling on the affected joints tend to go into spasm jamming the sore joint still tighter, and the muscles themselves ache unbearably with the cramp of their unrelieved contractions Almost every train arriving in Arizona

disgorges its quota of victims of this distressing malady, sufferers are less uncomfortable in dry climates

Dr Hench noticed that people with rheumatoid arthritis were frequently relieved of their pain when they had attacks of jaundice, while women sufferers were quite comfortable during pregnancy [19] This led him to believe that the condition was not wholly irreversible

The pituitary hormones build up in the blood of pregnant women This is the basis for the commercial isolation of the sex factors from pregnancy urine, since the large excess spills over into the urine Dr Louis Granirer recently demonstrated that arthritics can be benefited by injecting them with plasma made from blood that has been drawn from women forty-eight hours after childbirth [20] This was in line with Hench s observations

Gold salts have been used with varying success in the treatment of rheumatoid arthritis This occasional efficacy might well be explained on the grounds of some toxic effect on the liver, for when gold compounds are given to the point of intoxication, jaundice is a most prominent symptom—again commensurate with Hench's observations

In 1949 Hench treated several patients who had rheumatoid arthritis by injecting them with cortisone Within a few days the stiffness of their joints disappeared The pain was relieved and, in the course of a week or so, the swelling diminished There is a laboratory test used in the diagnosis of rheumatoid arthritis, in which the blood is treated to prevent clotting and then placed in a narrow-bored tube The corpuscles, being heavier than the plasma, settle in the tube In normal persons they will settle somewhat less than 20 millimeters in an hour In rheumatoid arthritics the sedimentation rate is several times as rapid In the cases treated with cortisone, the sedimentation rate became normal in a few weeks The muscle spasm disappeared but the anatomical changes in the bones and joints were not affected

It has been known that cases of rheumatoid arthritis sometimes have periods of spontaneous remission The patients Hench and Kendall treated felt so much better subjectively that these investigators feared the effect might have been purely psychic Without informing the patients, they substituted sterile salt water for the cortisone The symptoms returned within a few days When treatment was resumed with the drug the patients' symptoms again disappeared This proved that the hormone actually had the anticipated effect In treatment, the drug must be given indefinitely, since the symptoms return on its withdrawal[21]

The cortisone treatment was uniformly successful, and it earned for the discoverers the 1950 Nobel Prize in medicine, which they shared with Reichstein The same treatment was tried in cases of acute rheumatic fever which appears to be aborted by the drug,[22] but the investigators, with admirable scientific restraint, do not as yet claim that this treatment should supersede the older therapy with salicylates

Unfortunately the use of this drug is not unattended by serious danger In most of the conditions for which it has been used, there is no clear evidence of adrenal hormone deficiency Therefore, in treating with cortisone (or with ACTH, which causes the patient's own adrenal glands to secrete more of their hormones) we produce an excess of such adrenal hormone secretions—*hyperadrenalism* of at least a mild degree

There is a rare disease of the adrenal glands, Cushing's disease, in which the patient exhibits rather bizarre signs The face becomes round, the hair on the face and body increases (in both sexes), acne is commonly produced, a lump of firm fat grows on the back of the neck (the so called buffalo hump), fat is deposited around the hips, and there is increased pigmentation of the skin The female patient may stop menstruating There may be a diabetic condition Potassium is lost from the blood and sodium is retained There may be

high blood pressure Any or all of these symptoms may be produced either by excessive use of cortisone or ACTH or by their administration to a hypersensitive patient

In addition to these dangers, cortisone and ACTH have produced excessive coagulability of the blood so that clots may form within the blood vessels, i e , thrombosis An occasional patient has been rendered psychotic, and many of them are "euphoric"—they feel a happiness to which their state of health does not entitle them This euphoria, curiously enough, occurs in the final stages of tuberculosis, and has long been known as the herald of approaching death

Fortunately, most of these untoward symptoms disappear promptly on withdrawal of the drug Occasionally, however, the changes are permanent

Since ACTH is made from the pituitary gland it is almost impossible to keep all of the posterior pituitary out of the extract Some sensitive people have experienced transient episodes of extremely high blood pressure following each injection They have suffered severe abdominal cramps In a few cases the blood pressure has risen so precipitously that hemorrhages have occurred within the skull

Consequently it would be foolhardy indeed to administer these powerful drugs to those whose conditions already indi-

who have had indications of any condition associated with blood clots Persons with heart trouble should not take them, because of their sodium-retentive quality, which might induce heart failure

There is another effect of hyperadrenalism that might prove dangerous infection may occur without attendant fever (which warns of infection) For this reason the American Trudeau Society placed warnings in the press (December

4, 1950), advising that cortisone and ACTH not be used for tuberculosis and that arthritics be examined for latent tuberculosis before being treated with the drugs

A potential danger discovered only recently lies in the tendency of both drugs to raise the serum cholesterol[23] Since high cholesterol levels probably induce arteriosclerosis (opinion *still is divided*), one must reserve judgment as to the safety of the drugs when used over a long period While the blood cholesterol tends to decline *toward* its initial value after the drug is withheld for a time, it is possible that a dangerous process *may have been initiated*

These several considerations demonstrate the antagonism between the adrenal cortex and the islands of Langerhans The resultant drop in serum potassium has been recognized only recently as a dangerous condition It can cause muscle weakness, muscular irritability (manifested by twitchings), and often paralysis of muscles and changes in the heart[24] The muscle weakness first affects the trunk and limbs while in some cases the muscles of respiration are paralyzed, resulting in death When affected, the heart muscle becomes flabby and the beat is more feeble and rapid, while there are characteristic changes in the electrocardiogram

The bromidic statement that "support creates the need for support" is frequently valid, as, for example, *in the use of* cortisone When the natural secretion of cortisone is replaced or supplemented by externally administered doses, the demand on the adrenal glands decreases Consequently, when the drug is withdrawn, the glands may have reached a state of inactivity which in turn may result in a case of *hypo*adrenalism

Another objection to the use of cortisone stems from our uncertainty as to its being the *only* secretion of the cortex There is good reason to believe that the cortex secretes at least two and probably three hormones Administration of cortisone results in the circulation of that hormone alone For this rea-

son many clinicians prefer ACTH to cortisone, because ACTH stimulates the adrenal glands to produce more of its own hormones These hormones then are released into the circulation in approximately their proper proportions In excess, however, ACTH can produce the same ill effects as cortisone overdosage

In reconsidering the Houssay experiments, it will be remembered that the depancreatized animal failed to develop diabetes with the removal of the pituitary The phenomenon usually is ascribed to the removal of the pituitary itself It would appear possible, however, that diabetes failed to occur because the removal of the pituitary in turn *removed the stimulus to the adrenal glands*—which would have caused diabetes in the absence of the insulin of the pancreas While pure supposition, this concept is of considerable theoretical importance, because it coordinates many otherwise unrelated phenomena

In addition to its application to rheumatoid arthritis and acute rheumatic fever, ACTH has been tried for almost every condition for which we have no effective remedy While it has proved extremely effective in the treatment of bronchial asthma,[25] its results in other conditions are still too equivocal to reach a definite conclusion

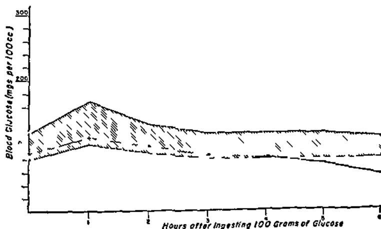
The symptoms of peptic ulcer as well as those of rheumatoid arthritis are temporarily alleviated during pregnancy [26] This, it is believed, results from the large amount of anterior pituitary hormones secreted into the blood Recently, however, ACTH and cortisone were tried in long-standing ulcer cases, but with disappointing results The patients showed signs of impending perforation, and operations had to be performed [27] This may have been caused by the known deleterious effect of these hormones on the blood vessels The drugs were tried in a few patients and in a large number of experimental animals All of the cases except one, however, were severe and of long duration The milder case responded

quite well, but the patient soon had the side reactions (buffalo hump and moon face), so that the therapy was stopped The ulcer symptoms then promptly returned The therapy would have received a fairer trial with less severe cases

The beneficent influence of pregnancy has its probable explanation in the glucose of the blood The glucose tolerance curve, it will be remembered, tends to be higher during pregnancy Because the large amounts of pituitary hormones circulating in the blood (as well as cortisone, which is increased by the stimulation of the adrenal cortex) are antagonistic to insulin, any excessive amount of insulin will be smothered The blood glucose, therefore, will tend to be higher, and conditions in which low blood sugar levels are found will tend to become milder

Burbank has noticed that arthritics have a tendency to low blood sugars, and the level tends to rise as they improve[28]

With this hypothesis in mind, a patient with rheumatoid arthritis was subjected to the six hour Glucose Tolerance Test The result?



12.—Rheumatoid Arthritis

This curve is typical for hyperinsulinism.

The patient had subclinical hyperinsulinism

If there is any merit to this hypothesis, the very first case tested must give such a result, for this theory cannot be based on a statistical study EVERY case must behave the same way If this test had not indicated hyperinsulinism, the entire project would have been abandoned Conclusions cannot be drawn from a single case, of course, and work to test the validity of our assumptions is now in progress On its completion, it will be reported in a standard medical journal [29] Naturally, we hope that we may be able to help arthritics along the same lines that have been so effective for the other conditions The treatment for hyperinsulinism does not depend on any scarce and costly drug, and it has the further advantage of not requiring hospitalization It would be wonderful if it succeeds But at this writing it must remain in the lap of the gods

In gout there is an impaired excretion of uric acid which piles up in the blood Treatment with ACTH or cortisone increases the excretion enormously and the symptoms clear up rapidly Withdrawal of either drug however, is followed by another severe attack [30] Gout is very rare in diabetics [31]

The Glucose Tolerance Test was given to a man who had [illegible]

[illegible]

tal. This will be done

8

Hyperinsulinism—
Key to Many Doors

SUBCLINICAL HYPERINSULINISM, CAUSE OR EFFECT?—MORE CASE HISTORIES—SUICIDE— MURDER— EPILEPSY— "CARES, DIFFICULTIES, AND TROUBLES"—THE GOLDEN KEY

WE HAVE INDICATED many bodily functions which can be affected by hyperinsulinism Our list may not now be complete, and time undoubtedly will reveal other [illegible]

ties, chronic partial starvation of the entire body produces difficulty in the operation of its parts Each cell in the body is affected to some degree We assign the effect to some specific part or system of the body because of our unavoidably limited comprehension of the problem Nature, however, does not suffer from the limitations of the human intellect, which can grasp but a few factors at a time Nature functions in accordance with *all* its factors Yet, while the entire human machine may be affected, it is possible that we may be aware of the misbehavior of only one or two parts

For this reason piecemeal treatment of patients so often is

unsatisfactory. When one ailment of the body is corrected, the patient may then notice other organs which have been out of adjustment, symptoms which had been overshadowed By nourishing all parts of the body at once, the entire being is brought into better adjustment Treatment should be fundamental

Often the question arises as to whether subclinical hyperinsulinism is the *cause* or the *effect* of accompanying illnesses It does not make any difference Such a cause-or-effect con-

[illegible]

duces its own effect But again, Nature does not function in this manner

Assume we have a certain amount of any gas in a suitable container Under specified conditions of temperature and pressure, it will occupy a definite volume If we raise the temperature, the gas will expand to occupy more space or, if we confine it in the same space the pressure will rise If we apply more pressure to the gas, it will contract its volume and it will get hotter If we allow it to expand by releasing the pressure, it becomes colder In all these changes we consider the change in pressure to be the cause of the changes in temperature and volume, or the change in temperature to be the cause of the changes in the remaining two, etc Pressure, volume, and temperature are so interrelated that only certain combinations of them can exist for any given quantity of the gas

Similarly, our concern as to whether hyperinsulinism is cause or effect is groundless We should recognize the fact that while the body can function under all sorts of conditions, we are so constituted that it operates most efficiently under rather rigidly limited conditions If we depart too much from the conditions to which we are adapted, our ease is impaired—we have dis-ease If we can restore the optimum conditions

for the operation of the body, it will accommodate itself to the new set of circumstances and will function with greater ease In all cases of undesirable functioning of the body ac-

tors adjust themselves to a new condition of equilibrium which we find more comfortable So the dis ease is eliminated Of course, we can reach a satisfactory point of equilibrium by other means We can administer ACTH or cortisone to coun teract the excessive secretion of insulin Or we can give drugs such as the belladonna preparations which depress the activity of the parasympathetic nervous system or those which stimu late the *sympathetic nervous system* (adrenalin, ephedrine, etc), in an attempt to reach a satisfactory balance We like our method—it requires no drugs Occasionally the need for drugs is imperative but when withdrawn the body must re adjust to the new conditions imposed by the withdrawal This second readjustment should not be applied to the body unless absolutely necessary Most routine cases do not require drugs

This account would not be complete without the inclusion of a few case histories to illustrate the application of the principles we have attempted to describe Some of these cases may defy specific classification, because they include symptoms of several different ailments

G M K is a prominent photographer For a number of years he had felt bad and had consulted more than a score of doctors He had symptoms of ulcer of the stomach, but X ray examination failed to confirm its presence He suffered from "sinus trouble" and coughed severely each morning He was deeply depressed and eventually found that his preoccupation with his symptoms interfered with his work. In 1948 he

reached the end of his endurance and made preparations to liquidate his business and retire to Arizona Under fifty years of age, the patient was resigned to a life as a crochety dyspeptic His symptoms, then, were gastric, allergic, and mental. The six hour Glucose Tolerance Test revealed the only condition which could account for these variegated symptoms hyperinsulinism After only three weeks on the Harris diet, his symptoms gone, the patient dropped his plans to retire and now, four years later, is still actively engaged in his work

B W is a housewife of forty five During her young adult life she had a toxic goiter which she tolerated for some twenty years because of fear of surgery Her condition finally became so severe that she submitted to an operation and recovered Soon, however, she began to gain weight and became terribly concerned about it She thought she could stifle the pangs of hunger by drinking several cups of black coffee each day

After a few months on this self imposed diet she noticed that she suffered from vague intestinal complaints At first these consisted of an occasional twinge of pain in the lower left side of the abdomen but soon the attacks became more severe Usually they occurred during the early hours of morning She consulted a physician, who naturally ordered an X-ray study of her intestinal tract His diagnosis was regional ileitis and he recommended an operation The operative procedure is quite formidable, for it requires removing a few feet of the last part of the small intestine and connecting the remainder to the colon The physician felt that the operation was urgent because by now the attacks occurred nightly, awakening the patient at about three or four o clock in the morning in excruciating pain

She consulted another physician who was aware of hyperinsulinism He examined her X rays and found indication of spasm of the bowel and not regional ileitis The X rays were then submitted to a roentgenologist of unquestioned emi

nence who agreed that there was nothing to suggest regional ileitis

A six hour Glucose Tolerance Test revealed hyperinsulinism, and B W was placed on the Harris diet Her attacks stopped within a week and have not occurred for three years —without an operation!

To repeat a word of caution if one wishes to take off weight by diet, coffee should be avoided, because the caffeine only temporarily stills the appetite by inducing a blood sugar increase Soon the islands of Langerhans become sensitized and once the insulin performs its function, the coffee's appetite-quenching qualities are most brief—and followed by a ravenous appetite!

P J, a woman of forty-eight, had suffered from claustrophobia (among other things) for fifteen years After a futile five-year search for relief from her "nervousness," she submitted to psychoanalysis—*for two more years Next she un*derwent a course of electric shock treatments, and for a year or so she was without complaint Soon, however, her memory returned, and with it her old phobias, plus a few new ones as well P J was exhausted Life no longer was attractive, and she considered suicide In desperation she tried another psychiatrist, and another, and yet another—all without success Finally *she yielded to family pressure and submitted to com*plete examination

P J revealed that for years she had eaten but one meal a day, in the evening Arising after the rest of her family had eaten, she simply could not bring herself to eat a solitary meal To appease her hunger she drank prodigious amounts of strong tea

Only one positive physical abnormality *was found* the characteristic tenderness and protective muscular spasm in the left upper abdomen The hyperinsulinism condition was

confirmed by the Glucose Tolerance Test, in which the blood sugar dropped to 63 within five hours With the blood sugar drop, P J felt faint, she reeled from the laboratory and wolfed down the usual postexamination glass of milk, following it with an enormous breakfast After the meal she felt better, and the nature of her ailment was discussed She interrupted the discourse with

"Doctor, did you say that I make too much insulin?"

"Exactly You have the opposite of diabetes"

"Then if I were given an injection of insulin, what would be the effect?"

"It would give you your usual symptoms with even greater severity" (As a matter of fact a large enough dose might even prove fatal)

"Well, three weeks ago the psychiatrist who was then treating me gave me two injections and after each one I felt the same way I did right after the test you gave me today I asked him what he had injected and he said he had given me small doses of insulin After the second injection I felt so weak I could hardly go home and I refused to continue the treatment And he didn t give me any tests He didn t even examine me!"

P J was given the usual treatment for hyperinsulinism Within a week she began to feel better, both physically and emotionally In two weeks she was able to travel alone, which had been impossible for years Today her anxieties are gone The improved somatic health has fortified her against anticipated mental strain

M H, a woman of thirty six, complained of fatigue, "nervousness," and irritability She could hardly attend to her household responsibilities, and she was always too tired to go out evenings with her husband After several years of searching for health, the patient received a Glucose Tolerance Test It was positive, and she was placed on the Harris diet, to

which she responded quite well She was amazed that she was not given any sedative medication she had exhausted the collection of barbiturates which had been previously prescribed for her nervousness

She complained, however, that *she must have her morning coffee* (three cups!), that she was "not fit to live with" unless she did She was advised that she would feel better and be easier to live with if she gave up coffee The patient did as she was told, she soon felt much better

At each visit she would ask how soon she might drink coffee and was advised that she should never drink it Moderate use of caffeine is perfectly harmless to the average person, once the insulin apparatus has been sensitized by overindulgence, however, coffee must be avoided

In a way, this is similar to the alcohol problem Moderate use of alcohol is not only relatively harmless but actually of help in withstanding the stress of civilized life If a person has been an alcoholic and conquered his craving, he must not take another drop

M H had to learn the hard way! She decided that one cup of coffee would do no harm, and for a while it did not In a few months, however, her symptoms returned—"butterflies" in the stomach, intestinal spasm, more nervousness She returned to the diet for a few weeks, had a few calcium injections, and again all was well

N K is a young World War II veteran A survivor of the infamous Bataan death march, he was a prisoner of war for more than three years, during which time he was systematically starved and beaten When rescued he weighed some ninety pounds, after several months' care in an army hospital he was discharged weighing about one hundred sixty pounds, his normal weight He continued treatment, however, attending Veterans Administration clinics regularly He complained of several varied symptoms In addition to those understand-

ably attributable to his digestive system he was jumpy and he suffered frequent nightmares in which he re experienced his prison-camp beatings He was referred to the neuropsy chiatric department where he was given a bottle of sedatives on each visit

Eventually the patient was given the Glucose Tolerance Test which revealed hyperinsulinism In addition to the Har ris diet he was given a few injections of calcium to boost his low blood calcium Within a few weeks he began to lose his nervousness and the nightmares disappeared To us it is obvious why he suffered the nightmares During the night his blood sugar would drop producing the sensation of hun ger, and by association he would relive his terrible prison camp experiences in which he had always been hungry Once the blood sugar drops were prevented he no longer had the nightmares Today he is well and vigorous in both mind and body

A B a member of an internationally prominent family came to America after undergoing the many vicissitudes of the chaotic war and postwar periods in Europe She was extremely shy and retiring and refused to associate with any of the young men who tried to contact her As a child she had had rheumatic fever and during the previous five or six years she suffered from serious heart trouble She was subject to severe attacks of tachycardia In addition she [illegible]

close the source of her condition Inevitably she was advised that her condition was psychosomatic that her physical diffi culties were primarily the result of her emotional difficulties While her physician refused to accept this theory he still was unable to supply another any more valid Finally A B came to Dr Richard Hoffmann who recognizing the possibil

ity of hyperinsulinism, suggested she place herself in the care of his associated internist—the medical collaborator of this book Investigation of her sugar metabolism corroborated Dr Hoffmann's suspicion, and with the Harris diet A B. fully recovered Her physical symptoms disappeared Her heart functions normally, except for one or two recurrences a year, when she treats herself by resuming the Harris diet for a week or two A curious effect of the treatment was the complete cessation of her besetting fears She has conquered her diffidence and has become interested in people She is about to be married And last year she reported spending an enjoyable summer vacation mountain climbing!

S M is a woman of sixty-nine who had been troubled with numerous allergies for many years She had a strong tendency toward hypochondria and had been seen by almost every prominent allergist She had positive skin reactions to almost one hundred allergens I (Dr Abrahamson) saw her for the first time when, following the use of a 'hormonal cream' at a beauty parlor, she had an allergic attack which caused her *face to puff up She was tested and found to have hyperinsulinism* After a few weeks on the Harris diet, her allergies disappeared But then she began to backslide and to eat sweets without restriction *Within a few days her hands be*came puffy and itched severely No external signs of irritation such as spots or redness, were visible She was given an injection of a calcium preparation and the puffiness *was relieved* overnight She was warned again about eating sweets

One day she ate some fish, with, as she put it, "fear and *trepidation*" She had almost always experienced *severe itch*ing and blotching of her skin a few hours after she ate fish This time, however, nothing happened She repeated the experiment with other varieties of fish, and with eggs, *to* which she was particularly sensitive What happened? Nothing Her allergies had completely disappeared So long as she

maintained her blood sugar level, *she could not have* ANY *allergies*

There are some sixteen thousand suicides each year in the United States We believe a great part of them to be preventable Many—perhaps most—of those who take their own lives are victims of the profound depression and ultimately irresistible urge to escape from life that so often is a manifestation of severe functional hyperinsulinism A few case histories may serve to substantiate this theory

E W is a woman of forty eight who is married to an indulgent, successful retired businessman twenty five years her elder Two years ago she became obsessed with the idea of having to go to work, both for financial security and to occupy the hours her husband spent at his club She became morose and then greatly depressed Her husband became ill and stopped most of his activities spending his time sitting in a chair as a semi invalid instead of at his club

One night while she and her husband were talking E W suddenly slumped from her chair and fell at her husband s feet The poor man was too feeble to move all he could do was to force a pillow beneath her head with his feet They were found the following morning the man crying helplessly, his wife scarcely breathing A doctor was summoned at once

Diagnosis was simple, an empty bottle of sleeping capsules told the story eloquently The patient was treated with intravenous injections of benzedrine every hour The physician gauged her return to consciousness by administering a "lifeguard s injection"—by pushing his thumbnail against the tender skin beneath the patient s thumbnail After a few hours this painful stimulus caused her to pull her hand away In another few hours her face contorted with pain Finally she stirred uneasily By evening she could be roused by face slaps, and was out of danger, able to sleep off the effects of

the drug Some thirty six more hours passed before she reached full consciousness

Both her husband and her doctor then realized that her protestations required serious attention She visited the latter after a few days and wept bitterly, demanding that she have something to do to fill the emptiness in her life Talk made no impression, finally her doctor assured her that he would arrange some work for her at a hospital—but first she had to be examined physically, to insure her ability to withstand the arduous work

The patient's eating habits had been abominable She feared obesity, and ate but one meal a day, her dinner, after drinking coffee all day long Such a diet almost guarantees hyperinsulinism E W had it, she was treated for it Her doctor, who never had any intention of finding her work, was never forced to refuse the request, for it was never made again The patient recovered from her despondency (and hyperinsulinism), she became energetic and gay She was able to help her husband through his serious illness, and their mutually better health has brought them complete happiness and understanding And although there are sleeping potions in the home for her husband s use, E W never uses them

A F is an artist in her early forties Two years ago she was stricken with lobar pneumonia from which she recovered, thanks to penicillin The increased load on her metabolic process, however had extracted its toll She began experiencing early morning and late afternoon weakness Her eyes were also affected, and she was forced to give up a portrait commission she had been executing She became terribly depressed She was given the Glucose Tolerance Test and found to have hyperinsulinism She was unable to follow the Harris diet, however, because she was living with a friend who ate and served a high carbohydrate diet She became *steadily* worse

Her husband had sustained severe financial losses She had hoped to redress the balance with her work—but she could not work Feeling useless and helpless, she no longer wanted to live The thought of suicide became an obsession She found and hid a bottle of sleeping medicine against the day when she could endure life no longer Her husband became aware of the disappearance of the medicine and was frantic At about this time they were at last able to move to their own apartment and so to go on the Harris diet They seemed to have turned the corner but their financial difficulties continued Her husband watched her for signs of improvement, always fearful that some crisis might detonate her urge to suicide At last he found the hidden bottle for which he had been searching He decided not to pour its contents down the drain but to test her death wish Suddenly he thrust the bottle into her hand and told her to drink it down, believing that he had called her bluff To his horror she put it to her lips and, before he could knock it out of her hand, she had taken a good sized swallow of it It was not a lethal dose and all she got from it was her first good night s sleep in weeks This proved to be the turning point Gradually, but with increasing effectiveness, the diet and treatment took hold of her Now, she is well on the way to complete recovery, all thought of suicide a thing of the past

M T, a man of forty-eight, had been brooding over domestic difficulties for many weeks A few months ago he concluded that he could no longer go on living, and compulsively drank a bottle of tincture of iodine He was rushed to a nearby hospital, from which he was transferred to the observation ward at Bellevue Hospital. His family asked Dr Richard Hoffmann to treat the patient, and four days after the suicide attempt he was released in Dr Hoffmann's custody During the next two days he was given the Glucose Tolerance Test, which revealed a hyperinsulinism condition—the blood

glucose fell to 55 in five hours The patient was placed on the Harris diet Within a week he reported feeling much better, fully capable of accepting his role in life and completely aware of the folly of his compulsive act Less than three weeks after the suicide attempt M T returned to work, feeling entirely fit He has since faced and resolved his domestic problems realistically and sensibly

Some of the more than eight thousand murders committed annually in the United States may also conceivably be due to hyperinsulinism We refer not to the gang murders, or those for greed, but to those committed without any satisfactory motive The murders that astonished Quentin Reynolds because they were committed by respectable people who had no prior police record—people who had never even received a ticket for a traffic violation Almost every day one can read of murder committed by someone whom psychiatrists now unanimously declare insane, but who prior to the event had been considered perfectly sane We know of only one such case in sufficient detail for discussion here, but it is typical of many

In 1947 Anthony Papa lived quietly on Long Island, a good and kind man respected by his community He had never committed a crime, never "been in trouble" One day a neighbor made disparaging remarks about Tony Papa's wife The remarks rankled Tony's pride He feared that the slur might be repeated and thus injure his good reputation He felt that he had to gain revenge from the neighbor, but he did not know how, and so he withdrew into himself and brooded about his lost prestige Had he any real impulse for revenge, he managed to control it for some time

One day, however, someone else taunted Tony about his wife, and the smoldering embers of revenge were rekindled. After brooding for some twenty four hours without food or

sleep, keeping himself alert with coffee, he decided to have it out with the neighbor He went to the man's house, only to find him gone For two hours Anthony Papa waited Then suddenly, without warning, he brutally killed the neighbor's five year old daughter

We do not intend to imply that Anthony Papa murdered because he had hyperinsulinism We do not know enough about such complex urges, nor do we know enough about hyperinsulinism s relation to murder, to make such an assertion Such speculation moreover, is beside the point

We do believe however, that the chronic partial sugar starvation of his brain cells prepared Anthony Papa for his act by fogging his moral sense distorting his normally realistic conception of his relationship to the world It will be remembered that the brain waves of persons with low blood sugar are abnormal It also will be remembered that a definite correlation has been established between low blood sugar as part of a general metabolic imbalance and certain types of insanity We know that a twenty four hour diet of coffee (caffeine) was made to order for what subsequently evolved It is hungry men who make revolutions, personal as well as social

Insanity is not a medical but a legal term A person legally is insane if he cannot distinguish between right and wrong and if he cannot understand the nature and quality of his acts In many murder trials the defendant will plead insanity in accordance with this legal definition If he is found to be sane, his counsel may attempt to establish the defendant s insanity at the time of the crime The prosecution invariably refutes such arguments and tries to prove in turn that the defendant is and was perfectly sane Both defense and prosecution utilize the services of various psychiatrists to prove their respective cases

Anthony Papa's attorney engaged Dr Hoffmann, who had appeared in similar trials, to examine the defendant and to testify as to his findings

Impressed by Anthony Papa's account of his day preceding the crime, Dr Hoffmann *requested* permission to submit the accused to a six-hour Glucose Tolerance Test I (Dr Abrahamson) performed this test *in the* jail at Mineola, in the presence of the Nassau County medical examiner The test indicated that Anthony Papa had hyperinsulinism!

Although they had little hope of convincing the jury of this discovery's significance the medical experts did their best to explain it in court, in the hope of pointing out that there was at least a reasonable doubt of Papa's complete sanity at the time of the commission of the crime It was impossible, however, to present such highly technical information convincingly The jury decided that Anthony Papa was guilty of first degree murder, and he was sentenced to die in the electric chair

Shortly before the completion of this book, the lay member of this collaboration became acquainted with "Narcotics Anonymous,' an organization patterned after A A and concerned with the rehabilitation of the narcotics addict The writer met a few of the members and gradually became aware of a rather peculiar habit common to them all carried hard candies to suck on When asked about this, one N A member remarked that "it seems to make it easier to do without the stuff"

On another occasion the lay member attended an open meeting of N A A young man who had been an addict for *only* two years was telling his story—how he had become a marijuana smoker and, after a while, having been told that "reefers" were *sissy* stuff, had taken up heroin

"Of course," observed the chairman of the meeting, "it wouldn't have happened if he hadn't been neurotic to begin with All of us are a bit neurotic or we wouldn't become addicts"

These two facts had a familiar ring A craving for the sol-

ace of sugar and the neuroses were old friends of ours by now Could it be that hyperinsulinism had something to do with addiction? The pieces fell into place morphine has an action similar to that of caffeine in causing a sudden rise in blood sugar The withdrawal symptoms of morphine—visceral colics, cold sweats, muscular and vascular cramps and collapse—are found in insulin shock

Our next step was obvious We must subject a few drug addicts to the six hour Glucose Tolerance Test

A highly intelligent and talented man of forty, L M has been using morphine for at least fifteen years Recently he "took a cure" Physical examination revealed the left upper abdominal tenderness and spasm associated with hyperinsulinism When given the Glucose Tolerance Test, L M's blood sugar fell from 92 to 58 mg of glucose per 100 cc in five hours L M said he felt as if he 'could use a shot" After breakfast the urge *apparently* was relieved

A B is an underprivileged, poorly educated boy of eighteen who was promoted to heroin from reefers during the past two years He voluntarily took the cure at the U S Government Hospital at Lexington, Kentucky During A B's Glucose Tolerance Test, his sugar tolerance curve followed a similar pattern, starting at 86 and dropping to 62 in six hours

Both patients were started on the hyperinsulinism diet Neither would cooperate, however, refusing to follow the diet and constantly missing appointments for calcium injections

We soon realized that proper investigation and treatment of this phenomenon is utterly impossible unless the patients are under rigid control We therefore are respectfully referring this problem to those government agencies having the patients and the means for such study

Among the signs and symptoms behind which hyperinsulinism masquerades, Seale Harris included those of *petit mal*

(mild epilepsy) It is significant therefore that some women who suffered from epilepsy appeared to improve during preg nancy as rheumatoid arthritis and peptic ulcer patients did—when the blood glucose tends to be higher Other pregnant epileptics however seemed to suffer more severely [1] A num ber of persons subject to epileptic seizures were given the Glucose Tolerance Test which indicated low sugar tolerance curves [2] It also has been found that the brain wave tracings of persons afflicted with petit mal were similar to those of hyper insulinism victims [3] While these facts are insufficient in them selves to indicate that epilepsy is a manifestation of hyper insulinism they provide enough evidence to warrant further investigation of the relationship between the two diseases

Less than two years ago Dr John A Schindler chief phy sician of the Monroe Wisconsin Clinic delivered an address over the University of Wisconsin s radio station WHA His remarks were published in the *Reader s Digest* (December 1949) and released to a shocked world

Fifty per cent of all the people going to doctors in the United States today are victims of this one disease" Dr Schindler stated Many would put the figure higher At the Ochsner Clinic in New Orleans a report was published re viewing 500 consecutive admissions to that institution of those 386 or 77 per cent were sick with this one disease"

What *is* this disease?

It used to be called psychoneurosis Dr Schindler went on Now it is known as psychosomatic illness And it *is not* a disease in which the patient just *thinks* he is sick The pain is often just as severe as the pain from a gall bladder colic

"Psychosomatic illness isn t produced by a bacterium or by a virus or by a new growth It is produced by the cir cumstances of daily living I have tried to find one word for it but it takes three each of them meaning about the same thing but in different degrees They are *cares difficulties*

troubles Whenever one has such a thick impenetrable layer of c d t that he can't get up above it into a realm of joy and pleasure occasionally, he gets a psychosomatic illness "

Cares, difficulties, and troubles are not far from Dr Portis' life situations which caused emotions to be relayed through the hypothalamus via the vagi to the islets of the pancreas, causing an oversecretion of insulin with consequent lowering of the blood sugar level We realize, of course, that Dr Schindler spoke before Dr Portis had reported fully on his findings and only a very short time after the medical member of this collaboration and Dr Hoffmann had reported on theirs For this very reason however—his apparent unawareness of the interrelationship of hyperinsulinism and the neuroses, and of the mechanism whereby life situations may contribute to setting up the vicious circle of hyperinsulinism—Dr Schindler s description of the symptoms of what is now called psychosomatic disease becomes all the more significant

Dr Schindler described the various parts of the body that are the first to reveal tension as a result of psychosomatic disease—the muscles at the back of the neck and at the upper end of the esophagus Then he tells us much more commonly the stomach is involved " He describes the pain as being "just as bad as an ulcer In our town we had a grocer who had a pain exactly like that of an ulcer He had plenty of trouble—a competitive business, a nagging wife a wayward son—and he had the pain most of the time Doctors assured him he had no ulcer He finally began to believe them when he noticed that every time he went fishing the pain disappeared And it didn't come back until he was almost home "

It will be remembered that persons with a real peptic ulcer as well as those who had no visible ulcer were both found to [illegible] on to say that the [illegible] " and when it did, [illegible] eale Harris listed appendicitis as one of the conditions under which hyperin-

sulinism masquerades Among many other *symptoms described* by Dr Schindler is the pain in the left upper portion of the chest to which we also have made previous reference *He also refers* briefly to ' the effect that the *emotion has on the* endocrine system "

While the usual therapy for the so called psychosomatic diseases is sometimes effective, we believe that the steadily increasing incidence of these ailments is patent proof of the insufficiency of such treatment We refuse to believe that Americans are becoming a people who "can't take it" We *prefer to believe that they are a people who have been beguiled* by a good deal of high pressure advertising into bad dietary habits and by an incredible lot of nonsense posing as science into bad living and thinking habits Admittedly they are also living through one of the greatest crises that has ever confronted *the human* race *It* is a crisis *that* impinges upon them at every angle of their individual and social lives It creates a plethora of emotion-arousing life situations What is needed is an understanding of their true nature and, for the individual who succumbs to them and to his bad habits and contracts this convenient psychosomatic disease, we humbly suggest a little more emphasis upon the *soma* and a little less *on the overworked psyche*

Specifically, we recommend to doctors and laymen alike in dealing with the psychosomatic, a thorough physical check up, *including the sugar tolerance test* It is high time that we realized that *blood sugar* is as important as an indication of health or disease as *blood pressure or blood temperature*

And should any of these psychosomatics prove to have the low blood sugar of hyperinsulinism, we respectfully suggest placing them on the proper diet to arrest it Then whatever psychotherapy is needed *will* be administered *more easily* They will begin to look upon the bright side of life for adult *reasons* and without undergoing the therapeutic bathos of a

cult of false and childish optimism, which our great nation is happily outgrowing

What have we been trying to say in this book? We have been trying to call attention to a condition that needs correcting The only reasonable authority on this earth is that of scientifically determined truths—truths upon whose secure foundations we can build things that work in useful ways

There is no greater evil on earth than ignorance of such truths when they are available That a condition, as far reaching as hyperinsulinism seems to be, should have been so long the stepchild of medicine is glaring evidence of the subtle retrogression of civilization in the past quarter century of bewilderment and vain search for short cuts and panaceas in every field

We do not say that all that we have written here is true We do say that we would not have written it unless we had *believed* it true It seems to us that the evidence we have presented points to the truth sufficiently to challenge others better equipped to investigate further into the facts we have rescued from the dark closet of professional and lay indifference

We believe that in 1924 Seale Harris discovered a golden key that will unlock many tightly closed doors We have indicated some of them There may be others Let us try the key in those many locks and see if the doors will open

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Notes

NOTE I, p 21

THE CHEMIST writes the formula for formic acid H COOH

The COOH group is known as carboxyl, the acid group It is composed of an atom each of carbon and hydrogen and two of oxygen

Acetic acid, CH_3 COOH, is next in the series The hydrogen has been replaced by CH_3, the methyl group The rest of the series have longer groups of carbon and hydrogen atoms Thus, proprionic acid, the third member of the family, is CH_3 CH_2 COOH

As the series continues the number of CH_2 groups in the line increases Hence, the fourth is butyric acid CH_3 CH_2-CH_2 COOH In combination with glycerin, butyric acid is butter fat

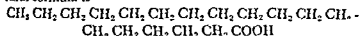
Eventually the series reaches stearic acid, which is found in tallow Its chemical formula contains sixteen CH_2 groups

There are, of course, other fatty acids in our foods Some of them do not consist of groups strung out in a single chain, they have side groups, like a lavaliere hanging from a necklace In others there is a deficiency in hydrogen For our purposes, *however, our attention is confined to the straight-*chained, saturated fatty acids

An added note of interest only those fatty acids with an even number of carbon atoms in their chains occur in our foods

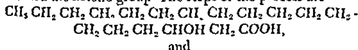
NOTE II, p 22

Let us consider the step-wise process of the burning of fats, taking stearic acid as an example Its structural formula is



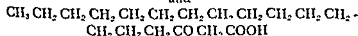
$CH_3\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2$ -
$CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,COOH$

In the body the second, or beta, carbon atom (atoms are labeled according to the Greek alphabet from the carboxyl group) undergoes oxidation and is changed into CHOH Oxidation then consumes the two hydrogen atoms of the new group, burning them to water (H_2O) and leaving CO, which is called the ketone group The steps of the process are



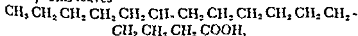
$CH_3\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2$ -
$CH_2\,CH_2\,CH_2\,CHOH\,CH_2\,COOH$,

and



$CH_3\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2$ -
$CH_2\,CH_2\,CH_2\,CO\,CH_2\,COOH$

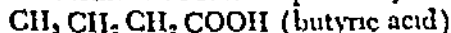
The last three carbon groups are readily oxidized the CO becoming COOH (the acid group) and the other two combining with oxygen to form CO_2 and H_2O (carbonic acid and water) This leaves



$CH_3\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2\,CH_2$ -
$CH_2\,CH_2\,CH_2\,COOH$,

which is an acid with two less carbon atoms

This process continues, the carbon chain becoming shorter by two carbon atoms with each step Finally we reach



$CH_3\,CH_2\,CH_2\,COOH$ (butyric acid)

The same process of oxidation of the beta carbon atom yields



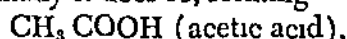
$CH_3\,CHOH\,CH_2\,COOH$ (beta oxybutyric acid),

and then



$CH_3\ CO\ CH_2\ COOH$ (diacetic acid)

This should in turn split off two carbon atoms like its predecessors, and normally it does so, forming



$CH_3\ COOH$ (acetic acid),

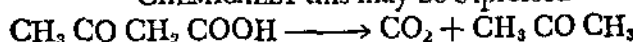
which is readily oxidized

Thus the fat is completely burned into carbonic acid gas and water

When carbohydrate is not burned completely, as in diabetes and also as in starvation, the last step in the burning of fat does not take place It is not known why this interruption occurs

NOTE III, p 22

CHEMICALLY this may be expressed



$$CH_3\ CO\ CH_2\ COOH \longrightarrow CO_2 + CH_3\ CO\ CH_3$$

References

CHAPTER 2

1 R H Major, ed, *Classic Descriptions of Disease* (Springfield, Ill, Thomas, 1932), p 186

2 *Ibid.*, pp 191–194

3 *Ibid*, pp 186–188

4 J Von Mering and O Minkowski, *Arch exper Path Pharm*, 26, 371, 1889

5 P Langerhans *Beitrage zur mikroschopischen Anatomie der Bauchspeicheldruse* (Berlin, 1869)

6 E L Opie, *Bull Johns Hopkins Hosp*, 12, 263 1901

7 F G Banting and C H Best, *J Lab clin Med*, 7, 265, 1922

8 K B Turner and E H Bidwell, *J Exp Med*, 62, 721, 1917

9 J W Gofman, F Lindgren, H Elliott, W Mantz, J Hewitt, B Strisouer, V Herring, and T P Lyon, *Science, N S 111*, 166 1950

10 D Adlersberg and O Porges, *Klin Woch*, 6, 2371, 1927

11 H P Himsworth and E M Marshall, *Clinical Science*, 2, 95, 1935

12 Himsworth, *Clinical Science*, 2, 117, 1935

13 J J Abel, E M K Geiling, C A Rouiller, F K Bell, and O Wintersteiner, *J Pharm Exp Ther*, 31, 65, 1927

14 H C Hagedorn, B N Jensen, N B Krarup, and I J Wodstrup, *J A M.A*, *106*, 177, 1936
15 L Reiner, D S Searle, and E H Lang, *J Pharm Exp Ther*, *67*, 330, 1939
16 F Bischoff, *Am J Physiol*, *117*, 182, 1936
17 F B Peck, *Proc Am Diab Assoc*, *2*, 69, 1942
18 C Krayenbuhl and T Rosenberg, *Rep Steno Mem Hosp*, *1*, 60, 1946
19 C Bernard, *Compt rend soc biol*, *1*, 60, 1850
20 B A Houssay, V G Foglia, F S Smyth, C T Rietti, and A B Houssay, *J Exp Med*, *75*, 547, 1942
21 R E Haist, J Campbell, and C H Best, *New England J Med*, *223*, 607, 1940
22 Von Mering, *Verhan Kong inn Med*, *5*, 185, 1886
23 J S Dunn, H L Sheehan, and N G B McLetchie, *Lancet*, *1*, 484, 1943
24 H J John *Endocrinology*, *18*, 75, 1934
25 W G Exton and A R Rose, *Am J Clin Path*, *4*, 381, 1934
26 L Hamman and I I Hirschman, *Arch Internal Med*, *20*, 761, 1917
27 H Gray, *Arch Internal Med.*, *31*, 241, 259, 1923

CHAPTER 3

1 S Harris, *J A M A*, *83*, 729, 1924
2 Harris, *Ann Internal Med*, *10*, 514, 1936
3 S H Gray and L C Femmster, *Arch Path Lab Med*, *1*, 348 1926
4 R M Wilder, F N Allan, M H Power, and H E Robertson, *J A M A*, *89*, 348, 1927
5 W R Campbell, R R Graham, and W L Robinson, *Am J Med Sci*, *198*, 445, 1939
6 A O Whipple and V K Frantz, *Ann Surgery*, *101*, 1299, 1935

7 Harris, *The Mississippi Doctor*, 13, 9, 1936
8 J W Conn and E S Conn, *Arch Internal Med.*, 68, 876, 1941

CHAPTER 4

1 Leonardo Botallo *Opera Omnia* (Leyden 1660), p 20
2 F A Simon, *Specialities in Medical Practice* (New York, Nelson, n d), p 303
3 *Ibid*, p 308
4 *Ibid*, p 303
5 *Ibid*, p 312
6 W T Vaughan, *Strange Malady* (Garden City Publishing Company, 1943)
7 A Q Maisel, "Allergies," *McCall's* (September, 1950)
8 A Myerson *Speaking of Man* (New York, Knopf, 1950)
9 Maisel, *op cit*
10 J H Black, *Texas State Med. J*, 39, 257, 1933
E P Joslin *The Treatment of Diabetes Mellitus* (4th ed, Philadelphia Lea and Febiger, 1928), p 733
H B Wilmer, M M Miller, and J T Beardwood, *Southern Med J* 29, 197, 1936
J T Malone, *U S Veterans' Bur Med Bull*, 5, 285, 1929
G L Waldbott M S Ascher, and S Rosenzweig, *J Allergy*, 10, 220 1939
11 R A Kern, *Trans Am Assoc Phys*, 49, 23 1934
12 Joslin, *The Treatment of Diabetes Mellitus* (6th ed, 1939), p 416
Joslin, H F Root, P White and A Marble, *The Treatment of Diabetes Mellitus* (7th ed, 1940), p 414
N Swern, *J Allergy*, 2, 375, 1931
Joslin, *The Treatment of Diabetes Mellitus*, 4th ed, p 734
13 L. Levi and H de Rothschild *La Petite insuffisance thyroidenne et son traitment* (1913), p 80

14 H A Rusk, T E Weichselbaum, and M Somogyi *J.A M A*, *142*, 2395, 1930
15 H R Sandstead and A J Beams, *Arch Internal Med*, *61*, 371, 1938
16 S Harris, *Ann Internal Med*, *10*, 514 1936
17 E M Abrahamson, *J Clin Endocrinol*, *1*, 402, 1941
18 J F Goodhart, *Albutt s System of Medicine*, *5*, 287, 1899
19 H W Barber and G H Oriel, *Lancet*, *2*, 1009, 1928
A V Stoesser, *J Allergy*, *3*, 332, 1932
A V Stoesser and M M Cook, *Lancet*, 58 12, 1938
20 A Prince, *N Y State Med J*, *40*, 1385, 1940
21 M M Peskin and A H Fineman, *Am J Dis Child*, 39, 1240, 1930
22 E L Ross, *J Biol Chem*, *34*, 335, 1918
23 F P Underhill and D H Sprunt, *Proc Soc Exp Biol Med*, *25*, 137, 1927
24 L Pollack and W Robitschek, *Wien klin Woch*, *39*, 753, 1926
25 R S Lyman, E Nichols, and W S McCann, *J Pharm Exp Ther*, *21*, 343, 1924
26 E M Abrahamson, *U S Naval Med Bull*, *40*, 711, 1942
27 *Ibid*
28 S A Levine, *Clinical Heart Disease* (1st ed, Philadelphia, Saunders, 1926), p 24
29 Joslin, *The Treatment of Diabetes Mellitus*, 4th ed, p 712
30 Abrahamson, *J Clin Endocrinol*, *4*, 71, 1944
31 A F Coburn and L V. Moore, *Am J Dis Child*, *65*, 744, 1943
32 E C Warner, F G Winterton, and M L. Clark, *Quart*

2371,

35 R E Rothenberg and L Teicher, *Am J Digestive Diseases*, *5*, 663, 1938
36 Joslin, Root, White, and Marble, *The Treatment of Diabetes Mellitus*, 7th ed , p 468
37 Himsworth and Marshall *Clinical Science*, *2*, 95, 1935
Himsworth, *Clinical Science*, *2*, 117, 1935
38 C R Stockard, *Medicine*, *5*, 116, 1926
39 Harris, *Am J Digestive Diseases*, *2*, 557 1935
40 J P Quigley, V Johnson, and E I Solomon, *Am J Physiol* , *90*, 89, 1929
41 Abrahamson, *Am J Digestive Diseases*, *12*, 379, 1945

CHAPTER 5

1 *S Harris, Ann Internal Med* , *10*, *514*, *1936*
Harris, *J A M A* , *83*, 729, 1924
2 C L Derrick, *Oxford Looseleaf Medicine*, IV, 178 (28)
3 E M Abrahamson, *Bull Reg Med Tech* , *1*, 138, 1940
4 R H Hoffmann and Abrahamson, *Am J Digestive Diseases*, *16*, 242, 1949
5 M Fabrykant and B L Pacella, *Proc Am Diabetic Assoc* , *7*, 233 1947
6 E H Parsons, E Ronzoni Bishop, S Hulbert, and E F Gildea, *Science News Letter*, *53*, 342, 1948
7 A T Cameron *Recent Advances in Endocrinology* (2d ed , Philadelphia, Blakiston, 1934), p 162.
8 *Harris, Ann Internal Med* , *10*, *514*, *1936*
Harris, *J A M A* , *83*, 729, 1924
9 T. A C Rennie and J E Howard, *Psychosom Med* , *4*, 273, 1936
10 S A Portis and I H Zitman, *J.A M.A* , *121*, 569, 1943
11 Portis and F Alexander, *Psychosom Med* , *6*, 191, 1944
Portis, J.A M.A , *126*, *413*, *1944*, *142*, *1281*, *1950*

Portıs, Zıtman, and C H Lawrence, *J A M A*, *144*, 1162, 1950
12 Portıs, personal communıcatıon to A W. P, August 3, 1950
13 W C Alvarez, *Ill Med J*, 83, 4, 1943
14 *Ibıd*
15 F Sondern, Jr, *Reader's Dıgest* (May, 1950), p 73
16 *Ibıd*
17 *Ibıd*
18 E F Lutz, *Ind Med*, 2, 599, 1946
19 S C Franco, *Ind Med*, *19*, 213, 1950
20 Portıs, *J A M A*, *126*, 413 1944, *142*, 1281, 1950
21 Alvarez, *Ill Med J*, 83, 4, 1943
22 Portıs, Zıtman, and Lawrence, *J A M A*, *144*, 1162, 1950
23 *Ibıd*

CHAPTER 6

1 C L Walker, *Harper's Magazıne* (July, 1950), p 29
2 M Mann *Primer on Alcoholısm* (New York, Rınehart and Company, 1950), pp vıı, 72
3 C C Furnas, *The Next 100 Years* (Baltımore, Wıllıams and Wılkıns, 1938), pp 156–157
4 L Hogben, *Scıence for the Cıtızen* (Garden Cıty Pub lıshıng Company, 1943), p 495
5 H Reılly, *Easy Does It* (New York, P J Kenedy and Sons, 1950), p 191
6 C H Durfee, paper read at a meetıng of the A A A S, December, 1938
7 Durfee, *J Crım Psychopath*, 3, 278, 1941
8 Durfee, *Quart J Stud Alc*, 7, 229, 1946
9 Durfee, *Rhode Island Med J*, *30*, 651, 1938
10 *Ibıd*, p 692
11 W B Farbsteın, *Fate*, *4*, 3, 1950
12 Reılly, *op cit*, p 275

13 W L Laurence, *Look* (July 18, 1950), p 53
H W Lovell, *Hope and Help for the Alcoholic* (New York, Doubleday, 1951), p 15

CHAPTER 7

1 C H Scott *Biological Symposia, 10,* 277, 1943
2 D W Bronk, *Science in Progress, Fourth Series,* ed George Baitsell (New Haven, Yale University Press, 1945), p 49
3 M Fabrykant and B L Pacella, *Proc Am Diabetic Assoc*, *7*, 233, 1947
4 R H Hoffmann and E M Abrahamson, *Am J Digestive Diseases, 16,* 242, 1949
5 B A Houssay, V G Foglia F S Smyth C T Rietti, and A B Houssay, *J Exp Med.*, *75*, 547, 1942
6 F G Young, *Lancet, 2,* 372, 1937
7 C H Best and N B Taylor, *The Physiological Basis of Medical Practice* (3d ed, Baltimore, Williams and Wilkins 1943), p 1160
8 W R Hess, *Schweiz Arch Neurol Psychiat*, *16,* 36, 1925
9 W W Swingle and J J Pfiffner, *Medicine, 11,* 371, 1932
10 E C Kendall *Trans New York Acad Sci*, *50,* 540 1949
11 C N H Long and F D W Lukens, *J Exp Med*, *63,* 465, 1936
12 F D W Lukens and F C Dohan, *Endocrinology, 30,* 175, 1942
13 D J Ingle, *Endocrinology, 29,* 649, 1941
14 T Reichstein and C W Shoppee, in *Vitamins and Hormones*, eds R S Harris and K V Thimann (New York, Academic Press, 1943), I 345
15 Kendall, *Trans New York Acad Sci*, *50,* 540, 1949
16 L H Sarett, *J Am Chem Soc*, *70,* 1454, 1948
17 Kendall, *Ann Internal Med*, *37,* 791, 1950

18 *Ibid*
19 P S Hench, *Proc Staff Meet Mayo Clin*, *13*, 161, 1938
20 L Granirer, lecture to the Society for Medical Jurisprudence, November 13, 1950
21 Hench, C H Slocumb, E C Kendall, and H F Polley, *Proc Staff Meet Mayo Clin*, *24*, 181, 1949
22 Hench Slocumb, Kendall, Polley, A R Barnes, and H L Smith *Proc Staff Meet Mayo Clin*, *24*, 277, 1949
23 D Adlersberg, L Schaeffer, and S R Drachman, *J A M A*, *144*, 909, 1950
24 J E Howard and R A Carey, *J Clin Endocrinol*, 9, 691, 1949
25 B Rose, J A P Pare, K Pump, and R L Stanford, *Can Med Assoc J*, *62*, 6 1950
26 Hench, *Proc Staff Meet Mayo Clin*, *24*, 167, 1949
27 D J Sandweiss, H C Saltzstein, S R Scheinberg, and A Parks, *J A M A*, *144*, 1436, 1950
28 Personal communication
29 Abrahamson *Am J Dig Dis*, on press
30 W Q Wolfson and C Cohn, *Proc of the First Clinical ACTH Conference*, ed by J R Mote (Philadelphia, Blakiston, 1950), p 241
31 Joslin Root, White, and Marble, *The Treatment of Diabetes Mellitus*, 7th ed, p 87

CHAPTER 8

1 S A Kinnier Wilson, *Neurology*, ed A Ninian Bruce (Baltimore, Williams and Wilkins, 1941), p 1526
2 G W J Mackay and H Barbash, *J Mental Sci*, *77*, *83 1931*
3 M Fabrykant and B L. Pacella, *Proc Am Assoc*, *7*, 234, 1947